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HISTORIC OUTLINE OF CARDIAC PATHOLOGY AND CLINICAL ASPECTS OF CHRONIC MYOCARDITIS.[1]

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I. Introduction.
II. Historic outline—Chronological Charts. Ancient Literature.
1. Morgagni, 2. Avenbrugger, 3. Corvisart, 4. Laennec.
III. Anatomy—Radiographs.
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VI. Ætiology.
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Introduction.

I have selected for our study to-night the disease of the heart muscle, a subject which to-day engages and in the past has engaged the attention of the best scientific investigators.

From the crude observations of Hippocrates and Galen to the scientific researches of our own time, we note the diligent search in the field of pathological histology, physiological chemistry, and physical diagnosis for more accurate knowledge of the ætiology and physical signs peculiar to this disease, whose onset is so insidious; whose destructive power is so subtle, and which is so frequently unrecognized until revealed by autopsy. When one observes at the autopsy table the frequency of myocardial disease unrecognized during life and the healthy heart muscle diagnosed in life as myocarditis, he is reminded of D'Alembert's story of the successful practitioner who, after conducting a prominent practice for thirty years, gave as his reason for retiring, that he was "weary of guessing."

It has seemed to me profitable to trace briefly the history

[1] A lecture delivered to the post-graduate classes of the Johns Hopkins University, May, 1903.

of the development of our present knowledge of cardiac pathology and especially of myocardial disease, for as Cook, in the preface of his translation of Morgagni, says, "the various steps in the progress * * * ought not to be disregarded, for, in difficult research, we derive encouragement from the recollection, that although the exertions of an individual may not advance philosophy in any perceptible degree, yet, owing to the power of experience, and the successive influence of opinion, the most obscure and apparently unsuccessful inquirer may prove the first or the connecting link in a series of the most valuable discoveries." (Cook's Morgagni, Preface.)

The following charts chronologically arranged will serve, if you follow them, as a guide through the historic data which I am about to give:

Chart No. I.

Historic Outline. (Chronologic.)

I. Epoch of Ancient Medicine. 1500 B. C. 300 A. D.

A. Greek Medicine.

460-377 B. C. ..... Hippocrates ..... Heart could not be diseased.

300 B. C. ..... School of Alexandria { Herophilus ..... Synchronism of Pulse and Heart Beat. / Erasistratus ..... Discovery of Valves and Explanation of their Function.

B. Roman Medicine.

1st Century Celsus ..... Heart Disease in Animals, in Man by Analogy.

131-210 A. D. Galen ..... Experimental Proof that Arteries contain Blood not Air.

II. Epoch of Mediæval Medicine 300 A. D. to 1400 A. D.

Human body not dissected from 300 A. D. to 1224 A. D. (School of Salerno) or possibly not till 1306 (Mundino of Bologna).

Ignorance ..... Superstition ..... Isolated Observations.

980-1036 Avicenna (Arabian Medicine) Peripheral Aneurisms.

In the epoch of ancient medicine (see Chart No. I) it is not till we reach Greek writings that any mention or hint of the heart as an organ subject to disease appears.

From the school of Alexandria (300 B. C.) we have a description of the valves and their functions by Erasistratus. Prior to this Hippocrates declared that the heart could not be diseased, thereby showing that the question of the possibility of its being diseased had arisen. In the Roman writings of ancient medicine—Celsus in the first century and Galen (131-210) in the second concluded by analogy from the diseased hearts of animals that man's heart may also be diseased, an observation which, according to Babcock, Galen made upon the athletes and gladiators. More important, however, than this was Galen's demonstration that the arteries contained blood not air. In the mediæval epoch (300-1400) anatomical research was spasmodic, and medical study, buried in superstition and ignorance, Avicenna's (980-1036) observation of peripheral aneurisms being perhaps the only one of importance. For sixteen centuries, a period extending from the epoch of the Alexandria school (300 B. C.) to the school of Salerno (1224), or more probably to that of Mundino (1306), the human body had never been dissected. (Chapman.)

Mundini or Mundino, professor of anatomy at Bologna during the latter part of the thirteenth century, "had dissected in eleven years only three human bodies" (Chapman). It is not, therefore, to be wondered at that the grossest ignorance prevailed.

Chart No. II.

Historic Outline—Continued. (Chronologic.)

Epoch of Modern Medicine ....1400-1900.

1440-1502	Benivieni	Anatomical and Pathological.
1511-1553	Servetus	Septum Imperforate. Pulm. Circ. Suspected and Described.
1514-1565	Vesalius	Aneurism of Aorta Diagnosed During Life. Interventricular Septum—"Invisible Pores."
1534	Massa	"Aneurism" of Heart, i. e., "Dilatation" and "Hypertrophy" of To-day.
1574	Fabricius	Valves of heart.
1590-1630?	Bonet	Fatty Infiltration or Degeneration of Heart Muscle.
1583	Cæsalpinus	Brief Description of Systemic Circulation.
1578-1657	HARVEY	CIRCULATION—PULMONARY and SYSTEMIC.
1597-1677	Glisson	Contractility of Tissue.
1628-1694	Malpighi	Capillaries.
1632-1723	Van Leeuwenhoek	Capillaries.
1638-1687	Steno	Muscular Structure of Heart.
1641-1715	Vieussens	Change of Apex Beat in Hypertrophy and Pericarditis.
1654-1720	Lancisi	Associates Asthma with Cardiac Disease.
1662-1738	Albertini	Recognizes Pulse of Aortic Regurgitation.
1666-1723	Valsalva	Anatomical Observations.
1682-1771	MORGAGNI	VALVE and MUSCLE LESIONS FULLY DESCRIBED. CASE OF ANGINA PECTORIS DESCRIBED—SYMPTOMOLOGY—PATHOLOGY.
1708-1777	Haller	Physiological Observations.
1722-1809	Avenbrugger	Physical Signs—PERCUSSION.
1755-1821	CORVISART	Physical Signs—WITH POST-MORTEM OBSERVATIONS.
1781-1826	LAENNEC	Physical Signs—AUSCULTATION.
1787-1872	Louis	Physical Signs and Symptoms—Acute Inflammation of Heart in Acute Disease—"Feuille Morte" Heart.
1768	Heberden	"Angina Pectoris" (term).
1776	Jenner	"Angina Pectoris," Coronary Aty. Sclerosis Suggested.

With the opening of the modern epoch (1400-1900) (see Chart No. II) anatomy was revived by Vesalius (1514-1565) and practical medicine and surgery were studied, and written upon by Benivieni (1440-1502) and Paré (1517-1590). From anatomical to physiological observations the steps were quickly taken. The valves and some idea of their function were more fully considered by Fabricius (1574), though the first study of these, as stated above, dates back to the school of Alexandria (Erasistratus, 304 B. C.). The pulmonary circulation was evidenced by the demonstration of the interventricular septum by Servetus (1511-1553) and by the declaration by the same observer that this septum was imperforated. The systemic circulation was considered by Cæsalpinus (1583).

Pathological observations, except for an aneurism of the aorta, diagnosed during life by Vesalius (1514-1565), an aneurism of the heart described by Massa (1534), were of little moment. The demonstrations of the systemic and pulmonary circulation by Harvey (1578-1657), of the capillaries by Malpighi (1628-1694) and Van Leeuwenhoek (1632-1723), of the muscular structure of the heart by Steno (1638-1687), of the contractility of the muscle by Glisson (1597-1677), and the general anatomical observations by Valsalva (1666-1723), make this hundred years the most important in the study of the anatomy and physiology of the

heart and blood vessels. With these great fundamental questions answered, Morgagni's (1682-1771) splendid observations, clinical, but more especially pathological, mark the beginning of another and very important medical epoch—that of clinical and complemental pathological study.

From Morgagni's "Seats and Causes of Diseases," in which is recorded his close observation, we have the first system of symptomology corroborated by post-mortem findings. Avenbrugger (1722-1809) contributes the first of the physical sign methods, that of percussion. Corvisart (1755-1821), the physician to Napoleon I, corroborates by post-mortem observations methods of physical diagnosis, while Laennec (1781-1826), with his stethoscope and method of auscultation, completes the list of prominent figures in this, which might be called the Epoch of Physical Diagnosis.

Close upon these, indeed almost contemporaneous, comes that great teacher whose influence went far to mould European and American clinical medicine—Piérre Charles Alexandria Louis.[2] The normal structure and function fairly well understood, the symptoms and the signs of disease formulated, and post-mortem findings in the normal and diseased observed and correlated to the symptoms and signs, the century opened with an opportunity for deeper study, which has been embraced with productive results to investigators on myocarditis, but least of all to the clinician.

In support of this statement, let me quote to you what Corvisart wrote of myocarditis and diseases of the heart in general—now nearly one hundred years ago (1806). Corvisart wrote, "The muscular substance is what most essentially constitutes the central organ of circulation. This acts the principal part in its organization—since to the contractility of the muscular fibre the motions are entirely indebted, which gave impulse to the fluid which the heart causes to circulate."

"This single view is sufficient to make us feel how alarming the lesions which necessarily induce the alteration and sometimes annihilation of the properties of the muscular fibre.

"Though there is some difference in the structure between the ventricles and auricles, the parietes of these cavities[3] *have not less dependence on the same muscular tissue.* In the healthy state, in fact, the particular arrangement of the fleshy fibres, and their inconsiderable number[3] *seem barely to distinguish the tissue of the auricle from the ventricle,* and it is in cases of great dilatations or other affections that the parietes of these cavities lose their muscular character assuming a membranous appearance, or suffering other changes. * * * Scarcely any disease of the heart is less known than carditis. Let one try to decide which is the real tissue affected, or to discriminate this affection from several others with which it may be confounded."

"Is the inflammation of the heart," Corvisart goes on to say, "always very sharp and acute, or does it not sometimes affect an insidious, hidden progress which it appears, if not impossible, at least very difficult to distinguish?"

Again, dilatation and hypertrophy are referred to as follows:

"In the first species (active aneurism) the heart is dilated, its parietes thickened, the energy of its action increased.

In the second (passive aneurism) there is likewise a dilation but an alternation of the parietes and diminution of the energy in the action of the organ" (pp. 75-76).

These very early works which I am enabled, through the courtesy of Mr. Brownne, Librarian of the New York Academy of Medicine, to show you, may be considered as the inspired writings of the four great evangelists of medicine—the inspiration of these *bearers of good news* being *close observation.*

STANDARD ANCIENT LITERATURE.

I. De Sedibus et Causis Morborum per anatomen indagatis (1762), Jo. Baptiste Morgagni (1682-1771).
TRANSLATION: Seats and Causes of Diseases Investigated by Anatomy—By William Cook, 1824.

II. Inventum Novum ex percussione thoracis humani at signo abstrusos interni pectoris Morbos detegendi (1761), Leopold Avenbrugger (1722-1809).
TRANSLATION: A New Method of Percussing the Human Thorax, etc.—By John Forbes, 1824.

III. Essai sur les Maladies et les Lésions Organique du Coeur et des Gross Vaisseaux—T. N. Corvisart, 1806.
TRANSLATION: By John Forbes, also Gates.

IV. De L'Auscultation Medical ou traite du diagnostic des Maladies des Poumons et de Coeur—R. J. H. Laennec, 1819.
TRANSLATION: By John Forbes, 1824.

I will not go further into the history of the study of myocarditis in our own times, as I shall have occasion to make use of many of the topics of this epoch in considering the different questions of myocardial disease. I refer you, however, to this table (see Chart No. III), and I think you will be struck with the absence of clinical observations in this, what might be called, the Epoch of Gross and Microscopic Pathology and Bacteriology.

CHART NO. III.

HISTORIC OUTLINE—Continued. (NOT CHRONOLOGIC.)
19TH CENTURY.

Hasse (1810), Rokitansky (1804-1878)..... Bochdalek, Dittrich, Virchow (1821-1902).	Pathological Observations.
Lobstein	"Arteriosclerosis" (term).
Gull—Sutton.....	do as a Disease.
Sobernheim (1837).....	"Myocarditis" (term).
Bamberger (1857).....	"Insufficiency of the Heart" (term).
Kreysig.	Heart Muscle Initial Seat of Inflammation.
Andral, Bouillaud, Bristowe, Frederick, Bard, Philipe.....	Interstitial Myocarditis.
Duplaix.....	Periarteritis and Extension by Proliferation of Connective Tissue from Vessels.

[2] Much valuable information in preparing the above was obtained from Chapman's "History of the Circulation of the Blood," Stengel's "History of Cardiac Pathology," Whittaker's "Article on Myocarditis" and many old books kindly supplied me by Mr. Brownne, Librarian of the New York Academy of Medicine.

[3] Italics not in original.

[4] An Essay on the Organic Diseases of the Heart and Great Vessel from Clinical Lectures of T. W. Corvisart, Gates' Translation.

Debove, Haushalter, Huchard, Martin.....	Arteriosclerosis of Heart.
Weber, Ludwig, Schmiedeberg, Schäfer...	Innervation of Heart.
Gunzburg, Wunderlich, Stokes	Acute Inflammation of Heart.
BIRCH HIRSCHFELD.....	Interstitial Proliferation. Gen'l Pathological Observation.
Leyden.....	Myocardial Inflammation; Acute and Chronic.
ROMBERG.....	Extensive Clinical and Pathological Observations.
Litten, Ziegler.....	Pyogenic Micro-organisms Cause of Myocarditis.
Councilman.....	Gonococci Cause of Myocarditis.
Allbutt, Meyers, Leitz, DaCosta.....	Muscle Lesions without Valve Lesions.
Bollinger.....	"Beer Drinker's Heart."
Loeb, Howell et al.....	Action of Inorganic Salts on Heart Muscle.
Krehl, Babcock, Gairdner et al.....	Clinical Contributions.

The epochs, as I have traced them, may be grouped as in this chart (see Chart No. IV).

Chart No. IV.

EPOCHS.

Prior to 400 B. C..	.....	Complete Ignorance.
400 B. C. 300 A. D.	Epoch of Anatomy No. 1..	Beginning of Accurate Observation—Anatomic Facts.
300-1500	.....	Decline of Anatomic Study—Superstition and Prejudice.
1500-1600	Epoch of Anatomy No. 2.....	Revival of Anatomy—Anatomical Laboratories.
1600-170	Epoch of Gross Pathology.....	Pathologic Study—(Gross), Pathological Laboratories—Symptomology and Morbid Pathology.
1700-1800	Epoch of Physical Diagnosis.....	Methods of Physical Examination—Clinical.
1800-1900	Epoch of Gross and Microscopic Pathology and Bacteriology	Pathological Histology. Bacteriology. Physiological Chemistry.

Each of the above represents the dominant consideration of its time.

Anatomy.

Just as effective treatment depends upon correct diagnosis, so correct diagnosis depends upon a knowledge of the normal and pathological anatomy and physiology. I will ask you then, before we consider the clinical phenomena of myocarditis, to review with me the more important anatomical and physiological points in the cardiac mechanism. Briefly, the heart structure is as follows:

I. Endocardium, smooth muscle and elastic tissue, includes endothelial layer which is continuous with endothelium of blood vessels.
II. Myocardium—(Referred to in detail below).
III. Epicardium—Connective tissue containing elastic fibres; under it is fat.

The myocardium is described by Szymonowicz[5] as a net work, consisting of two sets of fibres, a superficial and a deep. *In auricles* there is a separate deep layer and a superficial layer common to both. *In ventricles* the superficial layer runs at right angles to the deep layer. "The middle muscular layers of the heart are called by Krehl the 'driving mechanism.' These fibres run in circles and almost transversely around the ventricles forming, when separated from the rest of the musculature, a cylinder opened above and below. These transverse hooked-shaped fibres shorten the cavity of the ventricle, while the middle circular layers compress it. The papillary muscles and the columnæ carnæ shorten approximate and at length come into close contact —pressed together by the contraction of the circular layer * * * in consequence of the packing together and thickening of the papillary muscle, and fleshy columns during the systole; the extent of the contraction of the muscular walls required to empty the cavity is materially lessened, and their expulsive force is thereby economized. * * * The contraction of the ventricles proceeds in a twisting manner; the blood is, as it were, wrung out of the cavity. * * * *The community of the musculature determines the synchronism of the two ventricles."* (Schäfer.)

What interests us especially, then, is this muscular arrangement of the myocardium. The three layers:

1. Outer—runs right to left longitudinally.

2. Middle—runs circularly. "Driving mechanism" (Krehl).

3. Inner—runs left to right longitudinally; an arrangement which, together with the fact that "none of the strands of fibres begin and end in the same ventricle," and that they "terminate in the tendons of the papillary muscles," makes it of paramount importance to the proper function of the heart that the muscle be everywhere intact. I shall have occasion to speak of this arrangement again in the consideration of that important clinic phenomenon, arrhythmia.

The anatomy of the circulation of the heart will, I think, be appreciated by referring to this chart (see Chart No. V).

Chart No. V.

CARDIAC CIRCULATION.

Right coronary (smaller) (anterior sinus of Valsalva) divides into two main branches:
I. Descending—To each ventricle and ventricular septum.
II. Transverse—Approaches transverse branch from left coronary.

Smaller branches from these to:
Right auricle and ventricle.
1st portion of aorta.
Pulmonary trunk.
"Infundibular" over conus.
"Marginal" to apex and to posterior and anterior surface of right ventricle.

Left coronary (larger) (left sinus of Valsalva) divides into two main branches:
I. Circumflex (posterior transverse).
II. Descending (anterior).

These supply by separate branches:
Left auricle and ventricle.
Ascending aorta.
Left ventricle.
Both ventricles.
Vent. septum.
Pulmonary artery. Quain.

Right coronary—Circumflex descendens septi:
"End Arteries in Dog."—Porter.

Relative Sizes:
Smallest—1. Septi. Next—2. Rt. coronary.
*Next—3. Descending of Lt. C. *Anterior branch of. Largest—4. Circumflex of Lt. C.

"Smaller the vessel the least likely, if plugged, to cause arrest of heart." —Porter.

*No. 3 "Artery of sudden death."—Osler.

The most important clinical considerations are the anastomoses and the pressure. Porter says:

"Michaelis concludes that the coronary arteries are not terminal because a skillful injector has succeeded in making

[5] A Text-Book of Histology, Szymonowicz, page 83–131. Translated by J. B. MacCallum.

an injecting liquid pass from one artery through communicating branches to another. * * * *"

"No one," says Porter, "so far as I know, has denied that one coronary could be injected from another. Conheim himself makes special mention of the passage of liquids through the communicating branches under pressure. Everybody agrees that the coronary arteries anastomose. It is not the absence but the character of the anastomosis that is the basis of present pathological teaching. The incontestable fact is, that the anastomosis *is too slight to permit a collateral circulation sufficient to keep a vascular area alive after the closure of the artery which supplies it.*"

"The idea of terminal is physiological not anatomical. Terminal arteries differ from other arteries in that the peripheral resistance in the anastomosing vessels is too great to be overcome by the blood pressure in any of the arteries. * * * *The resistance in the communicating vessels and not their size is the factor of the first importance.*"[6]

In injecting these bullock hearts, radiographs of which I pass around (see Plate III) the following interesting point came up: Under 5 lbs. pressure, i. e., 10 inches or about 215 mm. of mercury, the injecting liquid (5% gelatin and cinnabar) was forced through the anastomosis. Under 3 lbs., 6 inches or 160 mm., it was not. I do not know what the blood pressure in the bullock is, but in the horse it is 11 lbs. 9 oz. (Kirke). This knowledge would enable us to say whether the anastomosis is only anatomical or physiological. (I wish to thank Doctor Sudler for his assistance and valuable suggestions in injecting these hearts.) The injection of the human heart under 130 mm. pressure (normal blood pressure) would or would not force the injecting liquid through the anastomosis, and we would obtain some information (in a relaxed heart to be sure) of the pressure needed to force the liquid through the anastomosis.

A word about the

INNERVATION OF THE HEART.

Though this is of great importance in the clinical consideration of myocarditis; in Schäfer's opinion the blood supply and intact muscle tissue is of more importance than the nervous machinery in the maintenance of the automaticity of the heart. The automatic action of the heart has been the subject of much study. From the important work of Brothers Weber in 1845 to that of Ludwig and Schmiedeberg in 1871, and of Schäfer in 1881, the consideration of the vagus and sympathic nerves as being concerned in the inhibition or in the augmentation or acceleration of the cardiac action has received much confirmatory experimental proof. Of the ganglia Schäfer[7] says (p. 200), "* * * The intrinsic cardiac ganglion cells belong to the same system as the extrinsic cardiac and vaso-motor ganglion cells, and there is no justification whatever for ascribing special central nervous system qualifications to the one and not to the other."

"The sequence of the contractions of the different parts of the heart," Schäfer goes on to say, "is not dependent upon the presence of the ganglion cells any more than the heart beat itself. *It is due to morphological differences in the muscles.*"

I shall have occasion to speak of this more fully when we come to consider clinically the heart sounds.

The nerve supply is remarkably rich as shown in Berkeley's beautiful specimens—in the Pathological Laboratory of this School. The question of the presence of a vaso-motor mechanism in the heart is an important one. Schäfer says, "Each systole does partially cut off the heart muscle from its blood supply, and at each diastole the injection of the coronary arteries aid in the dilatation of the heart. * * *

"Roy and Adami have shown[8] that vaso-dilators pass to the heart by the vagus, and vaso-constrictors by the sympathetic" —and Newell Martin has shown[9] that with excitation of the vagus and during asphyxia the coronaries dilate.

It seems possible to imagine that this vaso-dilatation could act during systole against the pressure of the contracting muscle and dilatation during systole—thus enabling the heart to utilize its blood supply. So important does this cardiac vaso regulating seem, that the fatal character of sclerosis of the coronaries with its terrible clinical phenomena are suggested as an inevitable sequence. An unstable vaso-motor mechanism, such as one sees in neurotics, would account for the palpitation observed in these people.

The blood pressure, according to Newell Martin and Sedgwick, in the coronary artery and aorta as shown by tracings synchronously taken, is identical for the aorta and the coronaries.[10] These are all facts of great clinical significance.

I must mention here what seems the most important contribution in physiology towards the clinical understanding of myocardial disease. I refer to the works of Howell, Loeb, Greene and others on the muscle contraction. While work on this subject was done prior to that of these observers —theirs has the most practical application. Stated briefly it is that variation in the quality and quantity of inorganic constituents of the circulating or surrounding fluid have different effects on the contractility of muscle.

The conclusion is that these inorganic salts play an important part in the automaticity and rhythmicity of the heart action. The great significance of these observations will be seen at once, and the knowledge of the chemistry of the blood of victims of myocardial disease becomes of immediate clinical importance. In this connection is the interesting fact that, "A strip from the mammalian heart, even when taken from the apex of the ventricle, will beat regularly at its own rate of rhythm apart from the beating of the rest of the heart;

[6] Porter: Jour. Ex. Med., 1896, Vol. I, pp. 55-56. Italics not in original.

[7] Text-Book of Physiology, 1900, pp. 182-188.

[8] Philos. Trans., London, 1892, Schäfer, p. 166.

[9] Trans. Med. Chir. Faculty of Maryland, 1891, Martin, p. 291.

[10] Quoted by Schäfer, p. 13.

provided that care be taken to keep intact the circulation of the blood through the coronary vessels supplying the strip."[11]

We see then that the—

I. The Muscle.
II. The Circulating Fluid.
III. The Vessels—and the
IV. Nerves.

} Must be considered in the clinical study of myocardial disease.

Pathology.

In the study of the pathology of the myocardium—probably the greatest researches and richest contributions on the subject have been made. While these studies have aided materially in understanding better the clinical phenomena, attempts have been made *to apply clinically the many pathological subdivisions of disease of the myocardium differentiable on post-mortem examination only.* Clinical research has, I think, been frequently bewildered in consequence.

Corvisart's statement with reference to subdivisions of "Carditis" may with advantage be quoted here. He says: "This separation of the affections * * * has in our time been extended much too far; the idea may be beautiful in theory, even great advantage may be derived from it in the study of the science, but in practice, it does not lead to useful conclusion."

I give on these charts clinical and pathological subdivisions from several authorities, and it will be seen that the statement above made is borne out (see Chart No. VI).

Chart No. VI.

Clinical and Pathological Subdivisions.

STRÜMPEL (Practice of Medicine).

I. Interstitial Myocarditis.
II. Idiopathic Hypertrophy (mechanical strain).
III. Acquired do (hypoplasia of aorta; resistance).
IV. Congenitally Weak Heart (ordinary demands too much).
V. Fatty Heart.

JAMES (Reference Handbook of the Medical Sciences).

I. Acute Interstitial Myocarditis.
II. Parenchymatous Deg. of Myocardium.
III. Segmentation and Fragmentation.
IV. Abscess.
V. Tuberculosis.
VI. Syphilis.
VII. Tumors.

WELCH (unpublished).

I. Acute Interstitial Myocarditis.
  1. Circumscribed.
  2. Diffuse.
II. Hyaline Necrosis of Myocardium.
III. Chronic Fibroid Myocarditis (with coronary arterial sclerosis).
IV. Fragmentation of Myocardium (with fatty degeneration).
V. Brown Atrophy.

OSLER (Practice of Medicine).

I. Coronary Artery Disease.
II. Acute Interstitial Myocarditis.
III. Fragmentation and Segmentation.
IV. Parenchymatous Degeneration.
V. Fatty Heart.
VI. Brown Atrophy.
VII. Amyloid Degeneration.
VIII. Hyaline do
IX. Calcareous do

} With clinical conditions corresponding to each.

Birch Hirschfeld.

Inflammation of Myocardium.
1. Acute pathogenic, probably never idiopathic.
  (a) Propagation from an inflamed neighboring tissue.
  (b) By embolism.
  (c) Infectious parenchymatous myocarditis.

Pathological Types.
  (a) Purulent myocarditis, often in connection with an ulcerous endocarditis; or with pyaemia (embolus), typhoid fever, rheumatism.
  (b) Diffuse infectious inflam. of the myocardium. In typhoid, diphtheria and scarlet fever.
  (c) "Myocardite Segmentaire" (Renaut).

2. Chronic (myocarditis fibrosa). In arteriosclerosis: arteriosclerotic myocarditis.
After infectious diseases: infectious myocarditis.
Krehl { In valvular lesions. Hypertrophy of the heart.
Syphilis.
Alcohol.
The Arteriosclerotic Myocarditis—In Spots.
" Strips.
" Spots and Strips.

Douglass Powell—(Allbutt's System).

I. Impairment secondary to general blood conditions.
II. Impairment secondary to altered blood-supply.
III. Impairment due to senile changes.
IV. Impairment arising from functional strain.
V. Impairment of inflammatory origin—Myocarditis.
VI. Growth.
VII. Parasites.

The division given by Birch Hirschfeld, like that of Welch, is more purely pathological, and that of Douglass Powell in Allbutt's System is more purely clinical, but in each instance a sharp line between the pathological and clinical is not drawn. The clinician is the greater offender.

It will be seen from these tables, that while a certain uniformity in the pathological consideration of myocardial disease exists—there is little to aid the clinician. The difficulty exists, I think, in not making a sharp distinction between those conditions which can be differentiated clinically—from those which can be detected by post-mortem examination only. If we make this sharp distinction the clinical list will dwindle materially. Following then Romberg, Rosenbach, Fraenzel and most German clinicians, the *clinical subdivision* on the first column of this chart results (see Chart No. VII).

Chart No. VII.

Subdivisions of Myocardial Diseases.

Clinical	Ætiological Factors	Pathologic.
ACUTE— Insufficiency of Heart Muscle with or without Valve Murmers.	ACUTE— 1. Fevers (acute) Typhoid, Diphtheria, Typhus, Small Pox, etc.	ACUTE— 1. Myocarditis, Interstitial or Parench. Deg.
	2. Pyaemia, Gonococci and other Pyogenic org's.	2. do
	3. Pericarditis (acute).	3. do
	4. Endocarditis (acute).	4. do
CHRONIC—	CHRONIC— A.—Diseases of other Organs and other Parts of Cardio. Vascular System.	CHRONIC—
	1. Arterio Sclerosis without Angina Pectoris.	1. Hypertrophy.
	2. do do	2. Coronary Aty. Disease.
		3. Fibrous lesions. Anæmic Necrosis. Septic Infarct.
	3. Angina Pectoris without General Arteriosclerosis.	

[11] Schäfer, p. 188.

Insufficiency of Heart Muscle with or without Valve Murmurs.	4. Endocarditis (chronic) Valvular Lesions.	4. Hypertrophy—Brown Atro'y.
	5. Pericarditis (chronic).	5. do Parench. Deg.
	6. Diabetes.	6. Fatty Deg.
	7. Nephritis (chronic).	7. Hypertrophy.
	8. Diseases of lung (chronic).	8. do Interstitial Myocarditis.
	B.—Systemic.	
	1. Old Age.	1. Fatty Deg. Brown Atro'y.
	2. Wasting Dis. and Cachexia.	2. do
	3. Obesity.	3. do Overgrowth.
	4. Phosphorus Poisoning.	4. do Deg.
	5. Alcohol.	5. Fibrous lesions.
	6. Syphilis.	6. do
	7. Interstitial Intoxication.	7. Parench. Deg.
	8. Beer Drinking.	8. Hypertrophy.
	9. Anæmia (acute and chronic).	9. Fatty Deg.
	10. Prolonged Fevers of Infections.	10. do Hyaline Deg.
	C.—Mechanical.	
	1. Strain (athletes)	Hypertrophy usually with some of the above.
	2. Overwork. Mt. Climbers Porters, etc.	
	3. Insufficient Exercise.	
	4. Congenitally Weak.	

Myocarditis Fibrosa may be in Spots, Strips, or both. Fragmentation and Segmentation may occur in Fibrous Lesions, Fatty deg. Infarction.

This commits us to no more than we can ascertain clinically. In considering the ætiology, as will be seen presently, this list can as Romberg suggests be extended without departing from clinical accuracy.

ÆTIOLOGY.

In considering the ætiology, it will be well to lay down the following broad laws:

I. Intact muscle and equilibrium of the nervous mechanism—are essential to rhythmicity of cardiac muscular action.

II. Equilibrium of nervous mechanism and rhythmicity of cardiac muscular action—essential to adequate and uniform blood supply to heart tissue.

III. Pure blood uniformly and adequately supplied are essential to proper metabolism.

IV. Any agent interferring with these essentials will cause:

1. Faulty metabolism.

2. Lowered resistance and remote consequence which, in themselves, may become factors in still further disabling the heart muscle.

This leads us to the consideration of many conditions (see Chart No. VII, second column), which, in former classifications, have come under pathological consideration, but which we may consider clinically without taking into account histological differentiations. These latter must not be neglected, but should not be introduced clinically *to the exclusion of signs and symptoms.*

It is impossible to discuss in a brief space disease of the coronary vessels and acute myocarditis—although these properly belong to this subject. Beyond brief reference to these I will not go, but refer you to Doctor Osler's monograph on "Angina Pectoris" and to the chapter on Arterial Sclerosis in Doctor Babcock's "Disease of the Heart and Arterial System"; also to H. Donner's "Ueber Arteriosclerosie," published in Stuttgart.

SPECIMEN.

This specimen, which was brought to my attention by Dr. Otto H. Schultze, is remarkable in that it shows slight myocarditis, with healthy coronaries, and was the heart of an individual who met sudden death due to plugging (as can be readily seen) of the orifice of the left coronary artery.

I will confine the balance of the paper to "Chronic Cardiac Insufficiency."

1. Hypertrophy without myocardial disease.

2. Hypertrophy with myocardial disease.

This cardiac condition, called also by Fraenzel "Idiopathic Enlargement of the Heart," comes on those past middle life, usually men who have led lives in which the essentials to good metabolism have not been supplied. Either the supply of blood has been vitiated by the introductions of poisons into the system, as alcohol in excess, syphilis, improper food; or the demands have been too great either through the muscular or nervous system, or both these groups of causes have been at work.

Gerhardt, Romberg, and Krehl are opposed to the view that overwork alone can act as a factor, while Dehio compares the process which takes place with overwork, to the dilatation of the abdominal walls in pregnancy, etc., but with the difference that the heart muscle can hypertrophy and thus compensate. When degeneration of the muscle accompanies this he refers to the theory (so extensively accepted some time ago), of the compensatory growth of connective tissue supporting the degenerating muscle fibre, which in time is replaced by connective tissue—with resulting cardiac insufficiency.[12]

Sluggish circulation due to sedentary life has been considered as an ætiologic factor, but Piery points out that sluggishness is only a condition favorable to the harmful influences of poisons and injections (alcohol, tuberculosis, rheumatism, etc.), and is not itself, as proven by experiment, capable of producing cirrhosis of liver and myocardial disease.[13]

Chronic interstitial nephritis is an undoubted factor. The work of Howell, Loeb, and others already referred to has given this factor a new importance. The inorganic constituents of the urine varying greatly as they do in nephritis would suggest the possibility of a regulating mechanism whereby those substances which produce muscle contraction are increased or decreased as the demands upon the muscle happen to be. This does away with the mechanical theory to a large extent. It presents many interesting questions and is worthy of careful clinical investigation.

Schneitz first called attention to diabetes as associated with

[12] Dehio: Schmidt's Jahrbücher der Med., 1891.

[13] Piery: Arch. Gen. de Med., lxxviii, 1900.

cardiac weakness, and considered the cardiac weakness more threatening than the diabetes itself. J. Mayer found in 380 cases of diabetes 82 with hypertrophied and weak heart muscle. Schott frequently detected glycosuria in patients in whom the condition had been overlooked by the physician sending the patient to Nauheim.[14] Heavy eating, heavy drinking, especially of beer (Bollinger), and a tendency towards obesity are potent factors in myocardial disease. The fact that excessive beer drinking is more commonly associated with myocardial disease, than excess in the use of other stronger alcoholic drinks, has raised the question whether the alcohol is the factor or not. I know of no satisfactory answer to this question, though many interesting theories suggest themselves. Romberg asserts that Havana cigars are more injurious to the heart than other brands. Syphilis and the congenitally defective system are also factors.

The psychological considerations, like the mechanical, seem to be secondary rather than primary factors. Worry, grief, anxiety, shock or fright, coming when the damaged muscle is doing its best, may prove just too much, and in this way appear to be the initial agents in a progressively failing heart.

The hypertrophied heart is considered on an experimental basis (rabbits) by Romberg and Hasenfeld to possess a reserve force equal to the normal, but such a heart cannot dilate as does the normal, and is therefore unable to stand strain.[15]

The frequency with which men of active mental habits and inactive bodies, men of large business interests, speculators, upon the soundness of whose judgment and the promptness with which it is given much depends, are victims of coronary and myocardial disease is a common observation.

The life of high tension, with often an undue license in times of relaxation, presents a combination of causes peculiarly suitable to the development of these diseases.

A stock broker, who with evidence of myocardial disease was under my care, described an attack, which he had upon the receipt of the news of Mr. Cleveland's Venezuelian letter, which would have seriously involved a large investment had he not in the short space of ten minutes manœuvred a transfer. His heart, he said, seemed to stand still, then as if bounding from his body plunged against the chest wall. He attempted to write some instructions, but had no control over his hands. He was able to ring his office bell and send for his secretary. Mechanically he instructed him, while his heart he described as fluttering like a frightened bird in a cage. He thought he was going to die. His secretary dispatched, he lay upon his office sofa, becoming as he thought unconscious. In ten minutes the secretary returned, and aroused his employer with the statement that the transfer had been successfully made, and that the news of the Venezuelian letter had spread "all over the street." It was about an half hour before his heart quieted down. This was two years before any other symptoms had developed, and five years before his death.

This is only one of a hundred such incidents as occur hourly in the speculating world, and it is not surprising that in such a business "Wine is mentioned in the bond." A few days ago, I saw in the Cornell Dispensary a case with pronounced arrhythmia dating from a shock received by the patient 12 years previously. The shock was produced by the sudden death of the patient's husband, of which the patient was a witness. The attacks of arrhythmia in this woman are paroxysmal, lasting about three weeks, and recurring about twice a year. The initial attack lasted about two months, and followed immediately upon the shock. I have notes of a similar case of three years' duration.

Symptoms and Signs.

In considering the symptoms and signs we can, I think, with profit return to Corvisart's division into 1st, 2nd and 3rd stages. It is to the 1st and 2nd stages that I would ask you to give special attention.

We are too prone to study the hospital cases and neglect the close observation of those minor ailments of private patients, and dispensary cases. Is it not here, if due attention be given, that heretofore unobserved signs and symptoms of the onset of this insidious disease will be detected?

Perhaps the first thing the well built, active man complains of is "is not feeling himself" and of "irritability" over small matters. These, to be sure, are complaints common to many conditions. They should not be unrecorded. Increase in weight when associated with even slight dyspnœa is an important symptom. This latter is often described as "feeling tight about the chest." Add to these, slightly disturbed sleep, numbness in the hands and feet, a lessened mental acumen, not the old time energy in getting to business, and the first stage may be considered complete. With the beginning of the second stage, it may be a few months or several years later, the patient decides to consult a physician.

We must now look to the clinical methods available. The nipple line as a landmark should be abandoned—it is too uncertain in our present pursuit for a more accurate method. The mid-clavicular line should be marked first; then the mid-sternal line; then the costal angle. With this done one may proceed to various observations.

Inspection.

A word about the heart movement as visible on the chest wall. "In man," Schäfer[16] says, "the pericardium is suspended above by the stout cords of the deep cervical fascia; below it is attached to the central tendon of the diaphragm in such a manner as to form a triangular box of considerable strength and rigidity. In this box the heart is slung. *Almost all lateral movement of the heart is thereby prevented*,[17] and since the central tendon of the diaphragm is a fixed point, the heart likewise cannot descend. It is agreed by nearly all observers that the apex does not move up to the base, but the base moves down towards the apex. The latter remains practically a fixed point."

[14] Schott: Wiener Med. Woch., 1899.
[15] Arch. Exper. f. Path. Med. Phar., 1897.
[16] Text-Book of Physiology, p. 6.
[17] Italics not in original.

"*The primary factor* (he goes on to say, page 35) *is the hardening of the muscular mass*," the secondary factor, the erection of the ventricles upon the base of the heart. The impulse is felt at a *different spot in each position of the body*" owing to the influence of gravity acting on the heart."

From these statements we see the point of maximum impulse depends for its character upon the activity of the muscular tissue; clinically therefore we must consider:

1. The position of the patient;
2. An impulse which may be felt, not seen;
3. An impulse which may be seen, not felt;
4. Entire absence of impulse to both touch and sight;
5. Wavy impulse;
6. Multiple impulses;
7. Impulses which have not corresponding beats at wrist.

1. Krehl reminds us that an absent impulse may be due to the maximum point being behind the rib.

2. The apex beat is often displaced without any disease of the heart (individual varieties).

3. We do not find a point of impulse when the intercostal spaces are too narrow; if the lung is thickened; in œdema; in emphysema of the chest wall, and in exudates of the pericardium, and Cabot [18] points out that—

4. The point of maximum impulse is produced not by the apex but by some part of the right ventricle.

5. The impulse which is visible and not palpable, I have seen in a case of incompetence with dilatation, but without murmurs. The diagnosis of myocardial disease had been made; autopsy showed mitral insufficiency with a normal myocardium. The case was seen for the first time in that deceptive stage of incompetency of valvular disease.

SPECIMEN: The heart I have here; and you will see that the myocardium is quite normal.

The observation of the P. M. I. and its character tells us little about the condition of the muscle unless taken in conjunction with other signs.

PERCUSSION.

The instrumental percussion has, I think, no advantages over the hand method; Sansom's pleximeter is the most satisfactory, though I have not employed the Ebstein glass pleximeter, for which much accuracy is claimed. The use of this latter in the method of palpatory percussion will be found fully described in Schwalbe and Ebstein's Hand Book and in the Proceedings of the Internat. Congress at Rome, 1894. Broadbent and Bezley Thorne claim much accuracy for the method of auscultatory percussion. Rather than advocate any one method, it is advisable to employ several, and it will be found that they either corroborate each other, or that a line is found confused by two methods and must therefore be considered uncertain. Moritz's [19] observations by radiograph are claimed by Ebstein to be not more accurate than by palpatory percussion. Karfunkel,[20] however, considers observations with the fluoroscope the surest method, and employs this in routine examination of the heart. Heitler states, as demonstrated by Giovani and Potain, that the relation of other viscera to the heart is clinically an important one. Heitler finds, with a large area of heart dullness, small pulse and a large area of liver and spleen dullness, and vice versa, that *if he strongly percusses or shakes the liver the pulse which was previously small immediately becomes large and full and the area of the heart dullness is decreased.*

A. Abrams [21] observed by means of the Roentgen ray that on rubbing the skin in the precordial region a contraction of the myocardium occurs. The myocardial contraction is more manifest in the left than in the right ventricle. The contraction is not sudden. In children it is about two minutes, and furthermore the cardiac recessions continue even after the source of cutaneous irritation is removed. This amounts to one inch on either side. This phenomenon is called by A. Abrams "Heart Reflex."

Abrams conclusions are: 1. Lung dilatation follows the exercise and bath treatment, the lung acting as an excretory channel for the overburdened heart.

2. The cause of the lung dilatation is dependent upon cutaneous irritation.

3. A decrease in the volume of the heart also ensues and is likewise provoked by cutaneous irritation (not by the vasomotor stimulation).

4. If in a given case of increased cardiac dullness, which has been carefully outlined, we vigorously rub the skin of the precordial region and note after a minute (the time for the abolition of the lung reflex) a reduction in cardiac dullness, we are justified in concluding that we are dealing with cardiac dilatation, and not with pericardial effusion. What is the value of the heart reflex, as an index to the condition of the myocardium? Valuable in this connection is the normally hyperresonant line from the left axilla to the umbilicus pointed out by Sir Wm. Gairdner.

AUSCULTATION.

It is, however, in the heart rhythm and sounds that we get early evidences of myocardial disablements.

Instruments more delicate than the stethoscope are needed, such as a clinical microphone. The phonendoscope is a crude instrument, but it is a step in the right direction. Oertel's stethoscope, which I will demonstrate presently, enables one to measure more accurately the relative intensity of the heart sounds.

Among the early signs arrhythmia and tachycardia are perhaps the most important. Musser [22] puts tachycardia, feeble, small pulse, dyspnœa and arrhythmia—the latter sometimes alone—as the most important early signs of myocardial disease. Krehl considers arrhythmia as pathogneumonic of

[18] Boston Medical Journal, Study of 196 Cases of Valvular Disease.

[19] Verhandl. der 18th Cong. f. Inner. Med. in Wiesbaden, 1900.

[20] Ztschr. f. Klin. Med., xliii, 1901.

[21] Med. Record, N. Y., 1901.

[22] Med. News, 1902.

myocardial involvement (see Figs. A, C, pp. 37-38). These signs then deserve special study.

Engelman, W. His, Jr., and Schäfer explain the different rhythmical power of different parts of the heart by morphological differences of the muscular tissue, and not upon the presence or absence of ganglion cells.

"The beat of the heart (says Schäfer,[23] p. 180) depends upon the (inherent) rhythmical power of its muscular tissue * * * some parts beat more easily than others, because their rhythmical power is greater * * * The sequence of the contractions of the different parts of the heart is due to a peristaltic wave of contraction, which starts from the most automatically rhythmical tissue and travels over the rest of the heart with varying speed, quickest over the tissue, which has become modified, so as to approach more nearly in its properties to ordinary striated muscle; more slowly over those parts which retain a more embryonic character, while at the same time, owing to the absence of modification of the tissue *between the auricles* and ventricles whereby it still retains its original more rhythmical but slower conducting power, the useful, purposeful pause between the auricular and ventricular contractions is brought about." And on p. 195 he says: "Any irregularity in the beat at headquarters will tend to be compensated by the time the ventricle contracts, so that the contractions of the ventricles will occur at much more regular intervals than elsewhere. Seeing that the main importance to the economy is to insure a regular ventricular beat, it is clear that this more or less complete obliteration of any irregularity in the rhythm by means of *the varying of conduction* at *different*[24] phases of the beat is a very important factor in maintaining the efficiency of the heart."

This is assuming that the muscle is intact; break any link in this chain and arrhythmia will result. The sequence of muscular contraction is from the auricles through the transverse fibres to the circular fibres and finally to the papillary muscles. The degree of arrhythmia will depend upon the portion of this muscular machinery, as well as the amount involved.

Radasewsky[25] compared in six cases the pathological lesions of the heart with the signs during life, and concludes that only in those cases where there was a diffused connective tissue degeneration of the muscles of the auricles was there irregularity and arrhythmia cordis. In those cases where the auricles were not much involved—even though the lesions in the ventricles were profound—the action of the heart was regular and rhythmical.

Krehl also calls attention to this association between arrhythmia and disease of the auricular muscle fibres, and explains it by a disturbance at the beginning of the sequence of the heart cycle. The results of arrhythmia and tachycardia Krehl sums up as follows:

1. Incomplete filling of heart chambers.
2. Overfilling of heart chambers.
3. Incomplete emptying of heart chambers.
4. Disturbed nutrition of heart.

I am following at present four cases of tachycardia—two alcoholic, which have continued at the rate of 120-130 per minute for three weeks, and two tobacco hearts, which ran between 100 and 120. There is more intermittency in the tobacco than in the alcoholic hearts. In one of the alcoholic cases there was no arrhythmia until the tachycardia had lasted for two weeks. In connection with the tobacco hearts, I would like to call attention to the possibility of poisoning from the constant handling of the dried tobacco leaf in making cigars and cigarettes. We have had several cases of what appeared to be tobacco poisoning, in which no other ætiologic factor presented itself. No reference beyond amblyopia is made to this, as far as I could find in Oliver's "Dangerous Trades."

The position of the patient while under examination must be carefully considered by the clinician.

Langowoy,[26] in a study of influence of the position of the body on the frequency of the heart beat says: "There is increased action in changing to the sitting position from the horizontal, because of the muscle work required in maintaining this position, because of the greater blood pressure on the heart and vessels, and consequent greater activity of the ganglia, and because of the greater pressure in the cranium with consequent irritability of the heart center in the medulla. In individuals with heart lesions, the heart action will be increased in changing the position from the horizontal to the vertical, as long as the ganglia retain their normal irritability. In some cases of insufficiency the normal irritability of the ganglia is not disturbed. In rare instances a disturbed irritability precedes the appearance of symptoms of insufficiency. In such cases the absence of an increase in frequency or even a diminution in the frequency on the patient assuming a sitting posture is a bad sign heralding an insufficiency."

The instruments devised for observing the various characteristics of the heart beat are many. The sphygmograph, the tonomotor, the pulse pressure gauge and the cardiograph are some of these. Of the cardiograph, Krehl and v. Frey are of the opinion that a unit of normal cannot be established even in one individual. The instruments of Oliver, Gaertner and Riva-Rocci for determining the blood pressure have been much used; the latter being the one almost exclusively used at present in Germany. This instrument has been reported on in this country by Cushing and Janeway. A very useful clinical modification has been just (February, 1904) devised by Janeway.

Bock (Munich),[27] by using the Oertel stethoscope, to which I have already referred, makes several valuable deductions (see Plate II). Bock was, with this instrument, able to

[23] Loc cit.
[24] Italics not in original.
[25] Ztschr. f. Klin. Med., 27, 1895.
[26] Deutsches Arch. f. Klin. Med., Bd. 58.
[27] Die Diagnosis der Herz Muscular Krankungen.

measure the *relative* intensity of the heart sounds in the healthy adult. His figures are as follows:

I. Mitral sound	40
II. Pulm. sound	18
III. Aortic sound	20

Thus the mitral normally has double the intensity of the aortic. In the neurotic heart, while the intensity of all the sounds is 2 to 3 times that of normal, each sound retains its normal *relative* intensity.

Bock analyzes the heart sounds in the following manner:

First sound: Muscular and valvular—accentuation depends upon the power with which the papillary muscles contract. Information about the muscles of the left ventricle especially is obtained from attention to this sound.

Second sound: Valvular—semi-lunars of the aorta and pulmonary artery. Accentuation depends upon the rapidity with which the valves close. The rapidity of the closure depends upon the pressure in the aorta and pulmonary artery. The pressure depends upon:

I. The power of the ventricles.

II. The resistance the blood meets.

At the aortic area—first sound tells of muscular power alone. Second sound tells us of a muscular power and valvular integrity.

A weak first sound at this area with an accentuated second sound would therefore suggest a feeble muscular power, or great arterial resistance.

At the mitral area—accentuated second sound occurs with fever, venus stasis, kidney disease, and circulatory disturbances in general.

In fatty hearts, with sclerosed coronaries, Bock calls attention to the (muskelgeraüsch) muscle sound—a rubbing, grating or scraping (schaben) which is not heard in fatty hearts without arteriosclerosis. This intramural murmur is a subject of great interest.

Krehl, in speaking of hypertrophy, warns against the conclusion that a weak first sound at the apex indicates a weak contraction, and gives as an example the hypertrophy with aortic insufficiency in which a weak first sound often occurs. This he explains by the slow contraction of the hypertrophied heart, the sound depending for its loudness upon the rapidity with which the heart contracts, and the rapidity with which the tension terminates. This explains why the first loud sound occurs in mitral stenosis and neuroses. The accentuations in hypertrophy he sums up as follows:

Hypertrophy of the right ventricle—accentuation of second pulmonic.

Hypertrophy of the left ventricle—accentuation of the second aortic with increased resistance of apex beat and strong pulse.

These then are some of the symptoms, signs and instruments by which we may detect the early stages of myocardial disease. In the third, or late stage, while there may be many signs and symptoms, yet the time for accurate observation has passed. How frequently are the murmurs of a well-marked valvular lesion entirely missing at this stage. So with myocardial disease, the confusions of sounds is such as to render their differentiation impossible. In this stage it is either sudden death from unrecognized myocardial disease, or the tumbling over heart; the Cheyne-Stokes respiration; the œdema all herald the end and are too confused for differential diagnosis. It is, therefore, in the first and early part of the second stages that we must seek for signs by which to make the diagnosis. It is at this time, as in the early stages of *pulmonary tuberculosis, that we may hope by treatment to aid our patient.*

PROGNOSIS.

In considering the prognosis Romberg divides chronic myocardial diseases into two stages: The duration of the first stage he places at from 10 to 23 years; variation in pulse and heart function with dilatation of the right and left ventricles takes place at this time. The second stage extends over a period of from 2 to 3 years. The average of 176 cases in this second stage was 14½ months. Morrisey[39] concludes from the study of 250 cases that the chief guides in prognosis are:

1. Efficiency of the heart.
2. Degree of hypertrophy.
3. Conditions of the organs other than the heart.

His advice is "give your prognosis on the best suppositions—treat your patient on the worse."

TREATMENT.

Of treatment I will say only a word. Perhaps in this diseased condition, as in many others, we take with advantage Napoleon's remark that "Life is a fortress * * * why throw obstacles in the way of its defense. Its own means are superior to all the apparatus of your laboratories."

The essentials of treatment may be summed up in the following: Rest, hygienic measures, encouragement, freedom from care, yet with pleasant occupation, exercise—active and passive. These pulse charts (Figs. A, C) show the variation in morning and evening pulse rate in a man with hypertrophy without valve lesions—also the effect of the resistant exercises upon the rate of the pulse.

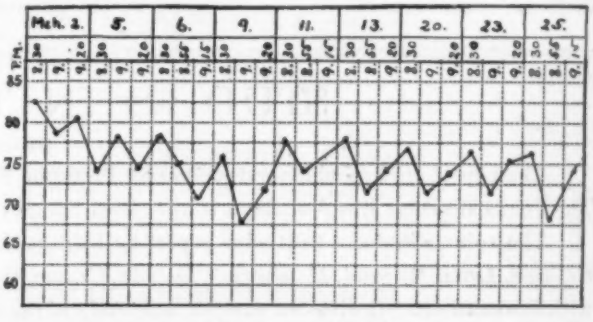

FIG. A.—Chart of evening pulse rate. Influence of 45 minutes of resistant exercises.

[39] Med. Record, 1900.

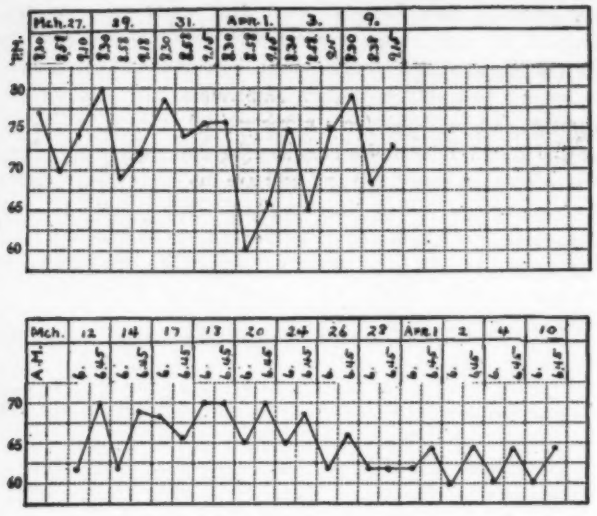

FIG. C.—Chart of morning pulse rate. Influence of 45 minutes of resistant exercises.

I show you here two charts representing the action of the Nauheim Saline baths given artificially (see Plate IV); you will see the striking change in the apex beat and cardiac outline. The principle of these baths depends upon a cutaneous irritation, which leads to a filling of the superficial vessels, with consequent relief to the congested heart and liver.

For a very thorough article on treatment, I would refer you to the chapter on "Treatment of Valvular Disease" in Doctor Babcock's book on "Diseases of the Heart and Arterial System."

"Cases," as Abernathy says, would probably "communicate more information in fewer words than descriptive or narrative," but unfortunately we must acknowledge even to-day Corvisart's statement made 100 years ago, "That a sufficient number of cases have not been collected to answer positively these questions; how does it happen," says Corvisart, "on dissection of some individuals that died of certain diseases * * * whose prognosis it is impossible to establish, how does it happen, I say, that, in such subjects the heart is observed in a morbid state which denotes actually a previous inflammatory diathesis, when the disease has presented in its progress neither signs or symptoms peculiar to simple *carditis?*" (pp. 73-74.)

There are many valuable modern writings on this subject which might be recommended; the following will, I think, be found standard and practical:

Schwalbe & Ebstein: Handb. der Prac. Med.

Babcock: "Diseases of the Heart and Arterial System."

Krehl: Nothnagel's System.

I acknowledge freely that this subject not even in one of its branches has in this brief space been covered. I shall feel, however, that our evening has not been misspent if I have aroused your interest in this subject of myocardial disease, and pointed out our great need for closer clinical observation. In closing I should like to emphasize the following:

1. The normal anatomy and normal physiology of the heart must be closely studied by the clinician.

2. The knowledge of the pathological anatomy and physiology is essential to clinical study.

3. The study of myocardial disease must be greatly extended by bedside observation. This can only be done by an honest limitation of our clinical conclusions to the evidence at hand.

4. The diagnosis must be made in the early stages of the disease.

5. Even with the best methods, the diagnosis of chronic myocardial disease at least is difficult, and its nature obscure.

Let me call your attention again to Chart No. VII, and urge the importance of conducting the clinical investigation from the *clinical viewpoint*, which the first column of this chart represents. The second column of the chart, that of ætiologic factors, represents in its relation to the first and third column the proper sequence of our inquiry; and in the third column appears the pathological probabilities. In the present state of our clinical knowledge of chronic myocardial disease we can consider only whether the muscle is *competent* or *incompetent*. Finer differential diagnoses, so commonly indulged in, are mere terms bewildering and dissipating the attention of the clinician from closer observation.

I can conclude with no better advice than that of Malpighi to his students: "Study nature and communicate matters of fact. Systems are ideal and mutuable, observations and experience are solid and unchangeable."

STUDIES IN TYPHOID FEVER.

SERIES I-II-III.

The papers on Typhoid Fever, edited by Professor William Osler, M. D., and printed in Volumes IV, V and VIII of The Johns Hopkins Hospital Reports have been brought together, and bound in cloth.

The volume includes thirty-five papers by Doctors Osler, Thayer, Hewetson, Blumer, Flexner, Reed, Parsons, Finney, Cushing, Lyon, Mitchell, Hamburger, Dobbin, Camac, Gwyn, Emerson and Young. It contains 776 pages, large octavo, with illustrations. It gives an analysis and study of the cases of Typhoid Fever in The Johns Hopkins Hospital for the past ten years.

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ILLUSTRATIONS OF OERTEL'S STETHOSCOPE FOR MEASURING THE RELATIVE INTENSITY OF THE HEART SOUNDS.

FIG. 1.—Stem of Stethoscope showing millimeter scales, one vertical measuring 40 millimeters, and one tranverse measuring 15 millimeters.

Outer and inner tube which can be moved so as to convert stem into a completely closed tube (Fig. 1) or into an open tube laterally (Fig. 2). This opening may be accurately measured by means of the vertical and transverse millimeter scale. Fig. 3 shows an opening of 3 square millimeters.

FIG. 2.—Same. Shutter entirely open forming open tube, opening measures 15 × 40 millimeters + 600 square millimeters.

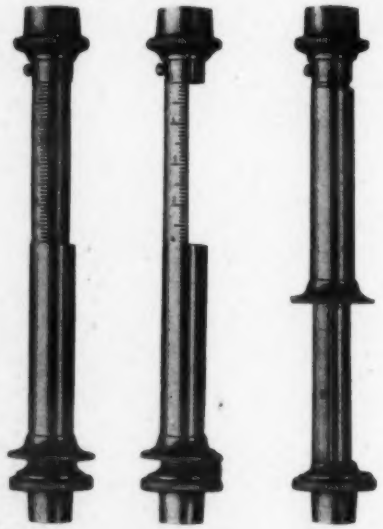

FIG. 1. FIG. 2. FIG. 3.

FIG. 5.

FIG. 6.

FIG. 3.—Same. Shutter partially closed, opening measures 3 square millimeters. The mitral sound is twice as loud as the aortic; i. e., at opening of 20 square millimeters aortic sound is no longer heard; at opening of 40 square millimeters mitral sound is no longer heard; at opening of 18 square millimeters pulmonary sound is no longer heard.

This does not mean that the normal heart sounds, in all individuals, are lost at these figures; it refers to the relation of the sounds to each other in an individual.

FIG. 7.

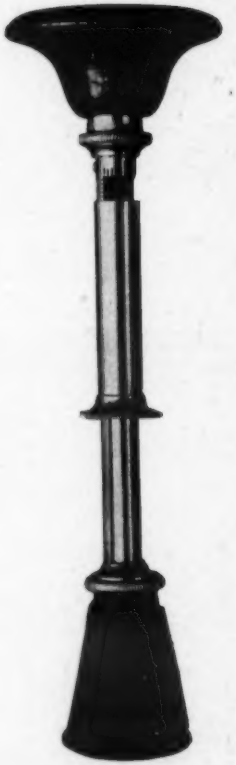

FIG. 8.

FIGS. 5, 6, 7, and 8.—Stem with various aural, etc., attachments.

Bullock's heart injected—right coronary—with 5% gelatin and cinnabar. Air pressure below 3 lbs., 6 in. mercury. Injecting fluid *not* forced through anastomoses to left coronary.

Bullock's heart injected—left coronary only—with 5% gelatin and cinnabar. Air pressure below 5 lbs., 10 in. mercury. Injecting fluid forced under this pressure through anastomoses into right coronary.

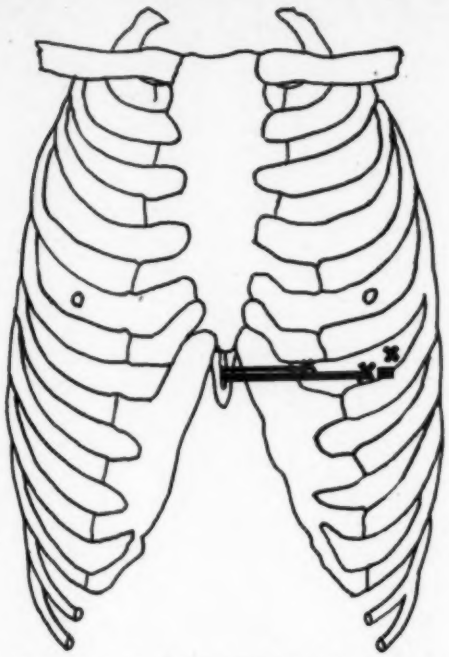

FIG. 1.—Hunt. Feb. 12. Before bath No. 1, strength No. 1. Point max. imp., 5th space, 13½ cm. from median line; after bath, point max. imp., 5th space, 11 cm. from median line. Feb. 13, no bath given. Point max. imp., 5th space, 10 cm. from median line. Feb. 14, bath No. 2, strength No. 1. Point max. imp. after bath 5th space, 8 cm. from median line. Feb. 15, no bath given. Point max. imp. not located. No signs (physical or post-mortem) of effusion.

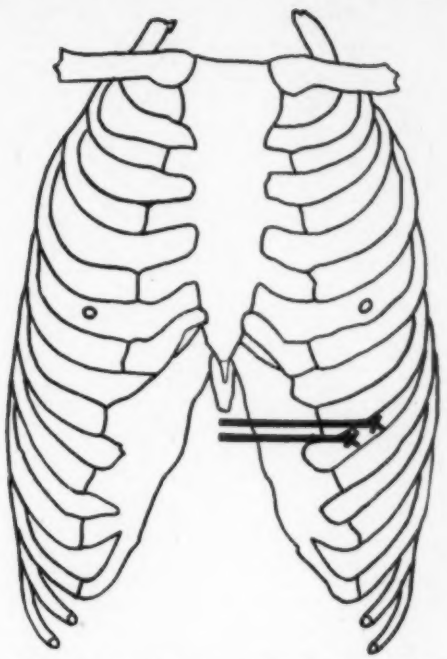

FIG. 2.—Larber. Before bath No. 1, strength No. 1, point max. imp. 14 cm. from median line. After bath, point max. imp., 12 cm. from median line. Length of time in bath, five minutes.

Figs. 1 and 2 illustrate the *immediate* influence of the baths upon the point max. imp.

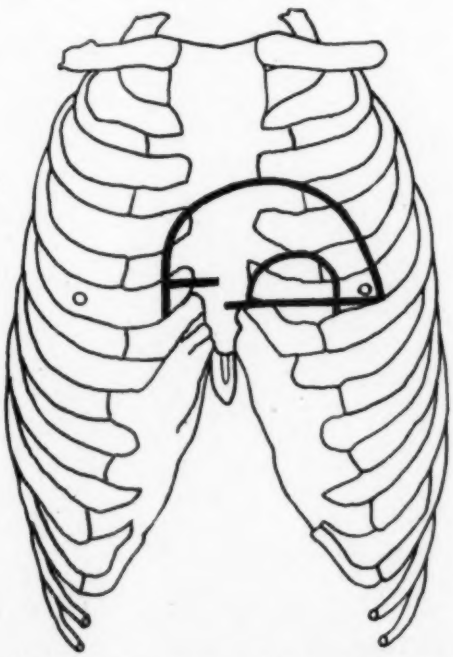

FIG. 3.—Coulbourn. Oct. 13, 1896. Cardiac outline before bath No. 1, strength No. 1. Right border 2¾ cm. from median line. In bath eight minutes.

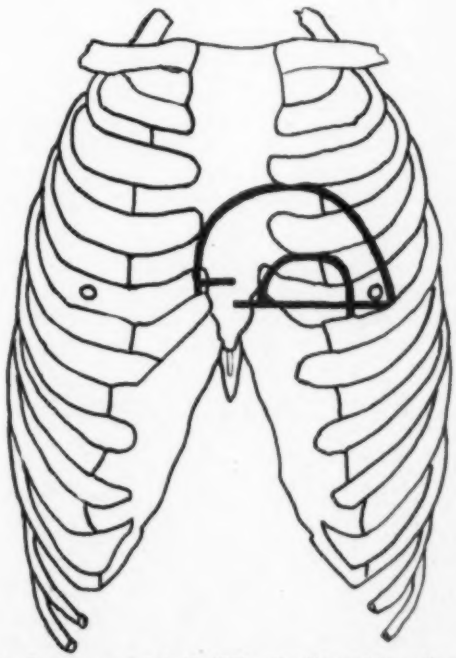

FIG. 4.—Coulbourn. Oct. 18, 1896. Cardiac outline after bath No. 6, strength No. 1. Right border 1½ cm. from median line. In bath eight minutes.

NOTE.—In Figs. 3 and 4 the outline on the right side of the chest extends too far laterally. It did not extend beyond the nipple. There was no change in this line after treatment.

Figs. 3 and 4 illustrate change of 1¼ cm. in cardiac area after six baths of strength No. 1.

FROM THE "SHOTT TREATMENT" OF CARDIAC DISEASE BY C. N. B. CAMAC, M. D.; J. A. M. A., AUG. 28, 1897.

THE EFFICIENCY OF THE PERIURETERAL ARTERIAL PLEXUS, AND THE IMPORTANCE OF ITS PRESERVATION IN THE MORE RADICAL OPERATIONS FOR CARCINOMA CERVICIS UTERI.

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A knowledge of the clinical efficiency of the blood-supply of the ureters is most important in all operations involving the ureter, and especially so in the more radical operations for carcinoma cervicis uteri. Clinical experience has taught us that the operative treatment of cancer of the cervix of the uterus has been unsatisfactory, for only about 12 per cent of the cases operated upon in this hospital are free from recurrence at the end of 5 years. (Statistics taken in October, 1902.) The only hope of bettering these statistics is by operating on the cases earlier, and doing the most radical operation possible in so-called favorable cases, for in these there is the best chance for a cure. The question arises: what is the most radical operation that can be done without too great a primary mortality? A study of the parametrium in those cases in which the more radical operation has been done shows that it is necessary to remove as much of the parametrium as possible, and that it is very difficult to diagnose clinically the presence of carcinoma in the parametrium, for the growth may metastasize to very small parametrial lymph-nodes, which may not have a diameter of over 1 to 1.5 mm., and cannot be palpated even after the specimen has been removed. From a study of the pathological findings, the indications of the operation which was described by me[1] over a year ago are only too evident. This operation consists in the removal of the lymphatics from the sides of the pelvis and with them the uterus and growth, en masse, and all the tissue from pelvic wall to pelvic wall. The question arises: What should be done with the lower ends of the ureters? If the lower 3-4 cm. of the ureters are removed with the growth and the renal ends of the ureters are implanted in the bladder there is danger of an ascending renal infection, for cystitis is an only too frequent sequel of such an operation. On the other hand, if the pelvic portion of the ureters are dissected free, ureteral necrosis may occur and at the same time the tissue has not been removed intact. I have done 11 of the more radical operations for carcinoma of the uterus, resecting one or both ureters in 3 cases. Three of the 11 cases have died, one on the 5th day from intestinal obstruction, and two from ascending renal infection, one dying on the 9th day and the other on the 17th day. In these last two cases the ureters were resected in one and not in the other. In the eight cases in which the ureters were not resected, they were dissected free as two cords and all the tissue from pelvic wall to pelvic wall was removed. Of these cases, one died of ascending renal infection, and ureteral necrosis occurred in one of the remaining 7 cases. These cases demand a better knowledge of the anatomy and physiology of the ureters and bladder and the etiological factors in the causation of cystitis, ascending renal infection and necrosis of the ureters. I have studied the etiological factors in the causation of renal infection and have published the results of these studies. In this article[2] attention was called to the importance of lowered local resistance and to the fact that injury to the kidney was a most important accessory etiological factor, and also that a stricture of the ureter was probably the most frequent cause of the lowered renal resistance. As cystitis occurs so frequently in these operations and as the ureter is implanted in a bladder which is very apt to become infected, the kidneys are not as well protected when the ureter is implanted as when it has its natural ureteral orifice. Nevertheless, as I shall try to show in this and subsequent articles, the advantages of the resected over the bared ureter are many, and as apparently the cystitis may be controlled by making a vesico-vaginal fistula, future clinical experience may decide in favor of the resection of the ureters. In eleven cases in which I have followed the bladder conditions after these operations, both by cystoscopic examination and by taking cultures, a marked cystitis has occurred in seven cases, in two of which it resulted in renal infection and death. In four cases the bladder appeared normal on cystoscopic examination, and yet in two of them when cultures were taken the colon bacillus was found present. An accidental vesico-vaginal fistula existed in three of these four cases and apparently controlled the bladder infection in these three cases.

The clinical efficiency of the blood-supply of the ureters must be understood whether one shall resect the ureters or dissect them free in these operations. Such knowledge can only be gained by a study of the blood-supply of the ureter, combined with animal experimentation and clinical experience.

THE BLOOD-SUPPLY OF THE URETER.

In reading over the descriptions of the blood-supply of the ureter, which may be found in the various Anatomies and other works dealing with the surgery of the ureter, one is impressed with the meagre account usually given, and the great variability of its source, for it is seldom that any two authors will agree, and furthermore very little seems to be known in regard to the efficiency of the blood-supply. This latter point is of the greatest surgical importance.

Quain[3] makes the following statement in regard to the blood-supply of the ureter: "The ureter is supplied with blood from small branches of the renal, the spermatic, the in-

ternal iliac, and the inferior vesical arteries. The veins end in various neighboring veins."

Morris[4] treats the subject a little more fully: "The arteries which supply the ureter are branches of the renal, the spermatic or ovarian, and the vesical; they anastomose freely together in the walls of the ureter, and the blood is returned by corresponding veins." In this manner one will usually find the blood-supply of the ureter disposed of in most of the Anatomies and in the surgical works on the ureter.

The best description of the blood-supply of the ureter which I have been able to find has been given by Disse.[5] According to him the arteries supplying the ureter come from many sources. The pelvis of the kidney is supplied by a branch from the renal artery which extends down over the abdominal portion of the ureter. The spermatic artery also furnishes a branch to the abdominal portion of the ureter as it crosses the ureter. The pelvic portion of the ureter is supplied by branches from the middle hemorrhoidal and inferior vesical arteries. These main arteries run along the ureter and are attached to its wall by loose connective tissue. The large arterial branches, visible to the naked eye, lie in the adventitia of the ureter and run in a longitudinal direction in such a manner that the ureter is encompassed by these vessels. From these larger vessels, branches arise at short intervals, which pierce the muscular coats of the ureter and extend to the propria; here they divide and give rise to small branches extending in a longitudinal direction from the bladder to the kidney. These small arteries are separated from the larger branches of the adventitia by means of the muscular coat. From the small arteries of the propria, capillary systems extend in two directions, one to the epithelium, and the other to form a capillary network inside of the muscular layer. The veins begin within the propria and receive the blood from the capillary network within this membrane. From these small veins, relatively larger vessels are formed which give rise to a venous plexus situated inside of the muscular layer. The main branches of this plexus lie principally in a longitudinal direction and are united together by other vessels. This is called the venous plexus of the mucosa. From this plexus the blood empties into still wider venous branches which lie in the adventitia, alongside of the main arterial trunks.

During the last year I made several experiments in order to determine the efficiency of the blood-supply of the ureter in human beings and the part played by each ureteral artery in nourishing the ureter. In five instances the arteries of the ureter for its entire length were injected by inserting a canula into the renal artery through the incised aorta, using an aqueous solution of Prussian blue in two cases and a 15 per cent solution of gelatine colored with ultra-marine blue in the other three. See Figs. I, II and III. In another instance the internal iliac artery was injected with a 15 per cent solution of gelatine colored with ultra-marine blue, and as a result the arteries of the ureter were injected for its entire length, and, on opening the kidney, a few small vessels in the kidney substance were found to be filled with the blue mass. Fig. V was drawn from this specimen. I have injected the internal iliac artery in another case, the ovarian in one, and the abdominal aorta in two, first clamping the renal and iliac arteries in the latter two cases, so that the coloring material could not enter these vessels. This latter group of cases was not quite as satisfactory as the first six cases referred to, as the work was done after the organs had been removed; nevertheless, they all demonstrated the free anastomosis of the arteries of the ureter giving rise to a periureteral arterial plexus and also that probably one could inject the entire plexus through any ureteral artery if the plexus were intact. Through this plexus there is established an arterial communication between the kidney and the bladder.

The periureteral arterial plexus from which the ureter is nourished is formed as follows: Branches, which we may call uretero-subperitoneal arteries, arise from the larger vessels, as the aorta, the renal, ovarian, iliac, uterine, etc., arteries. The source of these branches varies in different cases. See Figs. I, II, III and IV. These uretero-subperitoneal arteries usually divide into two branches, first a ureteral branch which helps to form the periureteral arterial plexus; second, a subperitoneal branch, which supplies the tissue about or near the ureter. The ureteral arteries on reaching the ureter divide into ascending and descending branches both running along the ureter, and united to it by loose fibrous tissue; the ascending branches anastomose freely with the descending branches of the ureteral artery above, and the descending with the ascending branches of a lower ureteral artery; thus there arise about the ureter, relatively large arterial trunks, running in a longitudinal direction from the kidney to the bladder. From these large trunks smaller branches arise which are more deeply imbedded in the perimuscular fibrous tissue of the ureter than the larger branches, and some of these anastomose with each other, thus forming, with the main trunks, a peri-ureteral arterial plexus extending the entire length of the ureter, up over the pelvis of the kidney and accompanying the ureter through the bladder. From this plexus, still smaller vessels arise which penetrate the walls of the ureter. In addition small twigs may arise from the plexus which leave the ureter to supply the tissue about it (Br. P. Fig. I), and these twigs may anastomose with branches of other vessels supplying these parts (Anas. Br. P. Fig. I).

The subperitoneal divisions of the uretero-subperitoneal vessels supply the tissue about the ureter and also, in places, the peritoneum. These vessels may anastomose with each other and with branches from neighboring vessels, including branches from the ureteral plexus, and thus may serve as a means of nourishing the ureter. The ureter may indirectly receive additional nourishment from other anastomoses, as the uterine and vesical arteries of one side anastomose with those of the other, and in addition there is a free anastomosis between the uterine and ovarian arteries and the branches from the latter anastomose with branches from the renal. The periureteral arterial plexus thus receives its blood-supply from definite ureteral arteries and may be nourished indirectly through the anastomosis of these arteries and branches from

the plexus itself with the branches of vessels supplying the tissue about the ureter.

It is easy to demonstrate the anastomoses of the vessels in the outer fibrous coat of the ureter. A very important question associated with the efficiency of the blood-supply of the ureter is to know whether or not there is a free anastomosis between the branches of the deeper ureteral arteries. In sections cut from specimens injected with Prussian blue the free anastomosis of the capillaries can be very easily demonstrated. On the other hand, I have never been able to demonstrate whether or not there was any anastomosis between the small arteries found within the muscular coats. These vessels are not very numerous and are very small, as is shown in Fig. V, where the internal iliac artery was injected with a 15 per cent solution of gelatine colored with ultra-marine blue. Ultra-marine blue being granular, only the arteries are injected, the granules being too large to pass into or through the capillaries.

From a knowledge of the blood-supply of the ureter it would seem that many liberties could be taken with the ureter without causing necrosis. As, for instance, the ureter could be dissected free from the bladder to the kidney, severing all vessels coming to the ureter between those organs, and yet necrosis would not occur if the periureteral arterial plexus was intact. Also in instances where the arteries supplying the ureter were tied, the anastomosis of branches from the plexus with the branches of neighboring vessels as well as the other arterial anastomoses which I have mentioned, would aid in maintaining the nourishment of the ureter. On the other hand, one would suppose that the destruction of the periureteral arterial plexus for only a short distance would lead to necrosis of the ureter, for even if there should be a free anastomosis of the deep arteries of the ureter, on account of their size and small numbers, one would not suppose that they would be capable of maintaining the nourishment of the ureter for any great distance. One must resort to animal experimentation as well as clinical experience in order to fully determine the efficiency of the blood-supply of the ureter.

EXPERIMENTS ON DOGS, DEMONSTRATING THE EFFICIENCY OF THE BLOOD-SUPPLY OF THE URETER.

The blood-supply of the ureter of the dog has been studied by several investigators. Margaroucci [6] thought that the principal source was derived from two small branches of the renal artery which accompanied the ureter as far as its opening into the bladder. Monari [7] has made some very interesting experiments in regard to the efficiency of the blood-supply of the ureter in dogs. He calls attention to the fact that the vessels supplying the dog's ureter run, in the perimuscular connective tissue, parallel to the ureter and are united to each other by numerous branches. He states that the ureter should not become necrotic when it is isolated for its entire length. He showed that the ureter of a dog could not only be freed for its entire length, but could also be free from the connective tissue surrounding it for a distance of 12-13 cm., and if replaced in this tissue necrosis could not occur. On the other hand, when he isolated the ureter for a distance of 6 cm. and placed gauze about it, necrosis occurred. Protopopow [8] has written a very extensive article on the anatomy and physiology of the ureter, in which he describes the blood-supply of the dog's ureter, calling attention to the free anastomosis of the vessels in its outer coat, thus demonstrating an arterial anastomosis between the bladder and the kidney. He states that he does not know if such a condition exists in human beings.

I have made several experiments in order to determine the efficiency of the blood-supply of the ureter in dogs. There is an arterial plexus about the ureter of a dog very similar to that found in man. It receives branches from the vessels near it and presents variations much as are found in human beings. The main trunks of this plexus tend to arrange themselves in two relatively large branches, one on each side of the ureter, which are loosely bound to the ureter. The smaller branches arising from these trunks anastomose with each other, thus forming the meshwork of the plexus, and are more closely united to the ureter than the larger vessels, as is also the case in man. On this account it is quite easy to injure the large trunks but not the smaller branches.

I. In seven dogs, the ureter was isolated for its entire length and an attempt was made to strip off the periureteral arterial plexus with my finger-nails. The dogs were killed in from 1 to 4 weeks and ureteral necrosis occurred in only two cases. In 5 cases the descending aorta was injected with a 15 per cent gelatine colored with ultra-marine blue, and very satisfactory injections of the ureter were obtained. It could be seen in these specimens that in trying to strip off the arterial plexus, I had removed only portions of the main arterial trunks and the large veins, while most of the smaller branches, which are imbedded more deeply in the outer coat of the ureter and form the meshwork of the plexus, were uninjured and were able, in five instances, to maintain the arterial plexus, and thus the blood-supply of the ureter.

II. In three dogs the ureter was isolated for about 4 cm. and in order to completely destroy the plexus, the ureter was scraped on all sides with a very sharp knife for a distance of 2 cm. Necrosis occurred in each instance.

III. In three dogs a ureter was isolated for nearly its entire length and then the larger vessels of the plexus were torn off by the finger-nails and mouse-tooth forceps, as in the first experiments. Both uterine vessels were tied, thus ligating the ureteral artery which completes the lower end of the plexus and arises from the uterine. Necrosis occurred in each instance.

IV. An attempt was made to simulate the condition sometimes found after the more radical operations for cancer of the uterus. In eight dogs the ureter was isolated for about its lower one-third and the tissue about it, including portions of the larger vessels of the plexus, were torn off as above. Both uterine arteries were tied and necrosis occurred in seven of the eight cases.

V. In two dogs the above was done, except the uterine ar-

tery on only one side was tied. Necrosis occurred in one case.

VI. In 25 uretero-vesical implantations in dogs, there was but one failure and that occurred in one of nine cases where organisms had been introduced into the bladder, in order to see the results of implanting the ureter in the presence of infection. In three of these nine cases the kidney became infected, and in each instance there was quite a marked stricture of the ureter at the seat of the implantation.

VII. In another dog the ureter was freed and stripped, as in previous operations. A small rubber tube, 8 cm. long, was split, and, by springing it apart, the ureter was placed within its lumen. Necrosis of the ureter occurred for a length of 7.5 cm.

It is evident that in a dog the ureter may not only be freed for its entire length, but its larger vessels may in part be destroyed by stripping them off, yet necrosis will not necessarily occur, for the plexus may be maintained by the smaller branches which are more adherent to the ureter and are very difficult to remove, and also by such portions of the larger trunks which have not been destroyed. On the other hand, when the ureter is scraped with a sharp knife, thus destroying the smaller branches as well as the larger, then necrosis will occur, even though the distance be very short. Again, when the ureter is freed but a short distance and the plexus interfered with, and in addition the arteries supplying the lower end of the ureter are ligated, then necrosis is very apt to occur; for the portion of the ureter stripped and also that below the injury, must receive most of its blood-supply from the blood-vessels in the plexus above the injury, and the stripping may interfere with the blood reaching these parts through the injury to the plexus.

In injury to the ureteral plexus, veins are destroyed as well as arteries, but as there is a very free anastomosis between the veins of the ureter, one would expect much less trouble from injury to the vein. Nevertheless, it must embarrass the circulation to a degree, varying with the extent of the injury.

Infection, exudates and foreign material, as gauze, must all be considered as accessory etiological factors in the causation of ureteral necrosis.

So far, the results of the study of the blood-supply of the ureter in man and experiments on animals tally. The next question which must be considered is what may be learned from clinical experience.

Clinical Cases showing the Efficiency of the Blood-Supply of the Ureter.

The clinical efficiency of the blood-supply of the ureter has been demonstrated by many operators.

In 1893, Kelly,[9] in attempting to remove the uterus in an advanced case of carcinoma of the cervix, ligated both internal iliac and ovarian arteries. The growth was not all removed and ureteral necrosis did not occur, although the left ureter was imbedded in cancerous tissue and was dissected free.

In 1896, Pryor[10] advocated the ligation of both internal iliacs in advanced cases of cancer of the uterus with the view of starving the growth. He refers to instances where these vessels have been ligated for other purposes and the pelvic organs have not been injured by the procedure. The following year he[11] reported a case where he ligated both internal iliac arteries for post-operative recurrence of carcinoma cervicis uteri in the vaginal vault. Necrosis of the pelvic organs did not occur.

Krönig[12] has reported three cases of extensive carcinoma of the cervix of the uterus, where he had ligated both internal iliac and ovarian arteries with satisfactory palliative results.

Iwanow[13] has reported five cases of inoperable carcinoma cervicis uteri where he had ligated the round ligament, the ovarian and internal iliac arteries with results similar to Krönig's cases.

From a review of such cases reported in the literature it becomes evident that the simultaneous ligation of the internal iliac, ovarian arteries and round ligament does not lead to necrosis of the ureters; for, as would be inferred from a study of the blood-supply of the ureter, as long as the arterial plexus is intact, necrosis would not occur. In addition, the other pelvic organs where the blood-supply has been injured by the ligation of these large vessels, would receive nourishment through the ureteral plexus, for by means of a canula inserted in the renal artery alone, one may not only inject the entire ureter, but also the uterus and bladder will be found to be partially injected. See Figs. II and III.

Cases may be found in the literature where the ureter has been freed for a long distance and yet ureteral necrosis apparently has not occurred.

Sänger[14] reports two such cases where the ureter was dissected free, in the removal of two intraligamentary cysts, without any apparent injury to the ureter.

Chrobak,[15] in the removal of an intraligamentary myoma, isolated the ureter for a distance of 8 cm. and at the close of the operation sutured the peritoneum over it and the patient recovered without any symptoms referable to the injury.

Rühl,[16] during a hystero-myomectomy, found that the ureter passed through an intraligamentary myomatous nodule for a distance of 7 cm. The ureter was dissected free and the convalescence was uneventful.

In 1894, Durante[17] removed a large adeno-cystoma of the ovary which was intraligamentary and had pushed the organs from the wall of the pelvis, including the left ureter, which was dilated to a diameter of 17-18 mm. It was found necessary to free the ureter from the kidney to the bladder. At the close of the operation the ureter fell back into the abdominal cavity like a loose cord. The convalescence was uneventful.

Frequently in this hospital the ureter has been exposed for long distances in the removal of intraligamentary cysts and myomata, and yet in not a single instance has necrosis followed such a procedure in these cases.

One realizes that when both internal iliac arteries are ligated, as in the cases above referred to, the arteries supplying the pelvic portion of the periureteral arterial plexus are destroyed, but necrosis does not occur, for the plexus is intact, and if so, it could probably be supplied by the renal artery

alone. On the other hand, when the ureter is dissected free, there is danger of injuring this plexus. Yet one realizes that still necrosis may not occur, for the plexus may not be injured, or such injury as may occur may be compensated by the smaller vessels of the plexus. Operators, both in this country and abroad, frequently ligate both internal iliac vessels and dissect the ureters free in hysterectomy for cancer of the uterus, and yet necrosis does not necessarily occur. On the other hand, necrosis of the ureters does sometimes occur in the more extensive operations for cancer of the uterus.

CLINICAL CASES SHOWING THAT NECROSIS OF THE URETERS MAY OCCUR.

There have been six instances of ureteral necrosis in 156 hysterectomies for cancer of the uterus in this hospital, and in each instance, in addition to ligating the uterine or anterior branch of the internal iliac artery or the internal iliac artery itself, the ureter has been exposed and dissected free. These procedures would not only probably cut off all vessels supplying the lower portion of the ureter, but by dissecting the ureter free the periureteral arterial plexus was also injured, thus interfering with the blood-supply coming from above. These cases will be reported in full in a subsequent article on ureteral necrosis.

Instances of ureteral necrosis following hysterectomy for cancer of the uterus may be found reported by several writers. Of interest are the cases of Wertheim.[18] He had five cases of post-operative ureteral fistula in his second series of thirty cases of hysterectomy for carcinoma cervicis uteri. Three of these cases were double, making in all eight instances. His operation consisted, first, in the isolation of the pelvic portion of the ureters from a point above their entrance into the parametrium down to the bladder. Thus the ureters were out of harm's way and a wide dissection of the parametrium was possible. The uterine arteries were ligated where they crossed the ureter.

At the instigation of Wertheim, Feitel [19] studied the blood-supply of the ureter in infants, especially as related to the operation of hysterectomy for carcinoma of the cervix. Feitel showed that the upper part of the pelvic portion of the ureter receives its blood-supply from the mesial side, i. e., from the aorta, the common and internal iliac vessels, and the lower portion receives its blood-supply from vessels lateral to the ureter, i. e., the uterine and vesical arteries. When it is necessary to expose the ureter, he advises that the upper part of the pelvic portion should be exposed by opening the peritoneum lateral to it, carrying the incision across the ureter, at the middle of the pelvic portion, and continuing down along the lower pelvic portion of the ureter mesial to it. Thus the nutrient vessels will not be injured. Wertheim,[20] in his next thirty cases, followed the suggestion of Feitel and did not dissect the ureter free as in the previous cases, but carried his dissection down mesial to the ureter, i. e., between the cervix and the ureter, in order to avoid vessels coming to the lateral side of the ureter. As a result of this procedure there were only two ureteral fistulæ in the thirty cases, as compared with eight in the previous thirty cases; and in these instances in which necrosis occurred the fistula resulted from *dissecting free the ureters, which were adherent to the growth, and thus he injured the periureteral arterial plexus.*

THE RELATION BETWEEN THE URETERS AND CARCINOMA CERVICIS UTERI.

In order to understand the difficulties in freeing the ureters in hysterectomy, one must undertand the anatomical relation between the ureters and the cervix of the uterus. If one will examine the ureters at autopsy, a very good idea may be obtained of certain anatomical features which are of the greatest importance in all operations involving the lower end of the ureters.

If the abdominal portion of the ureter is exposed and partially freed, and traction is made upon it, it can be drawn out from what is apparently a sheath, which seems to be derived from the subperitoneal connective tissue and is continuous with that surrounding the kidney above and accompanies the ureter into the pelvis below. Cross-sections of the abdominal portion of the ureter do not bring this out very clearly and it requires some play of the imagination to make out a definite sheath about this portion of the ureter. If the dissection is carried down into the pelvis, this apparent ureteral sheath becomes more definite, and cross-sections of this portion of the ureter show a definite sheath about the ureter which seems to be but a thickening of the pelvic tissue through which the ureter plays and is apparently continuous with the subperitoneal connective tissue about the abdominal portion of the ureter. In Fig. V, which represents a cross-section of the ureter taken about 1.5 cm. above the uterus, one can see the definite ureteral sheath and how it is apparently derived from the tissue about the ureter and acts as a protection to the ureter and the periureteral arterial plexus. If the dissection is carried on down to the bladder, the lower portion of the ureter will be found to be reinforced by muscular bundles which apparently extend up from the bladder over the ureter.

Waldeyer [21] has called attention to the fact that there is pictured in Krause's anatomy, longitudinal muscular bundles which extend from the bladder up to the ureter, but the cut is not accompanied with any description. Waldeyer describes them as longitudinal muscular bundles, which are united to each other by connective tissue and separated from the ureter by a space which can be injected. This sheath has a thickness of .5 to .75 mm., and he says extends 3-4 cm. up in the ureter. The lumen he considers to be a lymph-space.

Disse [22] refers to Waldeyer's sheath and says that these muscular bundles which are greatly hypertrophied, do not arise from the bladder as they appear to do, but from the ureter, and suggests that their hypertrophied condition as well as the space between them and the ureter arises from the contractions of the bladder pulling on the outer ureteral coat.

There are present about the pelvic portion of the ureter possibly two sheaths instead of one, the so-called sheath of Waldeyer, which Disse claims arises from a hypertrophy and

splitting of the outer ureteral muscular coat, and the second sheath, which apparently encircles the upper portion of the former sheath, blending with it, and extending upwards along the ureter. Further studies may show that this second sheath is but a continuation of the other, but from the few cases I have studied, it would seem to be different in origin, and although it blends with the other, it encircles the upper end of it, and extends further up along the ureter. The relation between the two sheaths needs further investigation. This latter sheath apparently arises from the tissues about the pelvic portion of the ureter and is continuous with the subperitoneal tissue surrounding the abdominal portion of the ureter. This sheath, which may be called the pelvic or ureteral sheath, is composed of fibrous tissue with an occasional muscle-bundle. Its lumen is, for the most part, filled with adipose tissue and fine fibrous tissue strands, thus acting as a cushion surrounding the ureter. One finds in the hardened specimens empty spaces which may be lymph-spaces, or possibly artefacts. This sheath is of great importance, for it not only furnishes a channel in which the ureter may slide as it contracts, but is also a protection to the ureter from the invasion of cancerous growths or inflammatory processes, and during operations in that portion of the pelvis. Of special interest in connection with this work is the fact that the periureteral arterial plexus lies within this sheath and is thus protected by it. See Figs. V and VI.

If one will study serial sections of the parametrium, one can see how adherent this ureteral sheath may be to the other structures in that part of the pelvis, especially the utero-vaginal and vesico-vaginal plexuses of veins, for it is from these structures that it is apparently partially derived. It is evident that the isolation of this sheath in the parametrial portion of the ureter is very difficult on account of its association with the structures above referred to, much more so than in that portion of the ureter above the parametrium, for here it lies just beneath the peritoneum and by freeing the peritoneum the ureter with its sheath may be moved about on the peritoneal flap. When the ureter is bared in these more radical operations, it is dissected out from this sheath and lies as a loose cord in the pelvis and there is the liability not only of necrosis from injury to the plexus, but the ureter has been deprived of its sheath and must now become fixed in scar-tissue, and thus its function will be interfered with and there is the opportunity for ureteral adhesions and partial or complete ureteral obstruction; and we realize how important an accessory etiological factor stricture of the ureter is, in the causation of renal infection. These statements have been confirmed by experiments on dogs and also, in one instance, where I made a uretero-vesical implantation for necrosis of the ureter, I found the ureter imbedded in dense scar-tissue.

What shall be done in hysterectomy for cancer of the uterus? Feitel and Wertheim solved the problem as far as the prevention of ureteral necrosis is concerned. When Wertheim removed the parametrium mesial to the ureter in order not "to injure the vessels supplying that portion of the ureter which comes in lateral to the ureter," he did something of still greater importance as far as the blood-supply of the ureter is concerned, viz.: that the ureter with its periureteral arterial plexus, as well as its sheath, is probably not injured. As stated, Wertheim did this in 30 cases and necrosis resulted in only two and in these the growth had extended out to the ureters, making it necessary to bare the ureters and thus the sheath was not only destroyed but the plexus was probably injured sufficiently, to cause necrosis of the ureters. We realize that when the parametrium is involved either by a direct extension of the growth or by metastases, it takes but very little involvement to go to or beyond the ureters, as I shall show in a subsequent article; therefore, when Wertheim did a hysterectomy mesial to the ureters and also removed the pelvic lymph-nodes, the intermediate tissue between the primary growth and the pelvic lymph-nodes about or lateral to the ureter had been left behind.

If one were sure of the prevention of ascending renal infection, the resection of the ureters would be the most rational procedure, for the ureters could be cut off just as they enter the parametrium 1.5 cm. below the place from which illustration, No. V, was made and afterwards the peritoneal flap carrying the ureter with its sheath could be carried down to the bladder, and after implanting the ureter into the bladder, the sheath with the peritoneal flap could be sutured to the bladder, and thus the plexus would be uninjured and the ureter would be provided with a sheath which could help to prevent stricture and protect the blood-supply of the ureter. In addition, all tissue from pelvic wall to pelvic wall could have been removed and with it the early extension and metastasis of the growth into the parametrium. Some may claim that when the parametrium is involved either by direct extension or by metastasis, the case is hopeless. If so, the vaginal operation is the one of choice in all cases. This statement needs confirmation, and it is too early to make any definite statements either way, and the more radical operation is demanded on the basis of the pathological findings and the results of the less radical operations. If the cystitis and ascending renal infection can be controlled by making a vesico-vaginal fistula and if the implantation can be made without too much tension, thus avoiding a stricture, then this is the operation of choice, for it offers the greatest chance for a cure. The suturing of the ureteral sheath and the peritoneum to the bladder will undoubtedly in great measure relieve the tension of the implantation.

The dissecting free of the ureters is difficult, more so than resecting them. While there is less danger of ascending renal infection there is a greater chance of ureteral necrosis. A hysterectomy mesial to the ureters offers less chance of a cure than the above and also little danger of either ascending renal infection or ureteral necrosis.

Conclusions.

1. The ureter is nourished by a periureteral arterial plexus, the main trunks of which run in a longitudinal direction, from the kidney to the bladder, in the outer loose perimuscular

fibrous coats of the ureter. From these longitudinal vessels, smaller branches arise, some of which anastomose freely with each other, thus forming the mesh-work of the plexus. These smaller branches are for the most part more deeply imbedded in the outer coat of the ureter than the main trunks, which in places may be but loosely united to the ureter.

2. This plexus is nourished mainly by the ureteral arteries which arise from branches of large vessels along the course of the ureter, as, the aorta, the renal, ovarian, iliac, uterine, and other arteries. The ureteral vessels are not the same in all cases, as a branch from one artery, as for instance, the ovarian, present in one case may be absent in another and its place taken by a branch from another artery, as the aorta, a ureteral branch of which may not be present in the first case. See Figs. I, II, III, and IV.

3. The plexus may receive additional nourishment from small branches arising from the plexus, which supply the tissue about the ureter and may also anastomose with the branches of other vessels supplying these parts.

4. It is possible to inject the entire plexus from such arteries as the renal and internal iliac, and also probably from any one artery which furnishes a ureteral artery.

5. The ureter with its plexus is protected by the tissue in which it lies, and in the pelvis this tissue is converted into a definite sheath, which is apparently derived from the tissue through or along which the ureter passes. This sheath acts as a protection to the ureter and its plexus from the invasion of cancerous growths and inflammatory processes, and should be recognized in all operations involving the pelvic portion of the ureter.

6. Animal experimentation shows that many liberties may be taken with the ureter and even when the plexus is injured that the blood-supply of the ureter may be maintained by the smaller branches of the plexus which are more deeply embedded in the outer coat of the ureter than the larger vessels, and so are more difficult to injure. The ureter of a dog may not only be dissected free for its entire length, but even the plexus may be injured and yet necrosis may not occur. On the other hand, the complete destruction of the plexus for only a short distance, or the partial destruction of the same, which ordinarily would not cause necrosis if combined with the ligation of the vessels supplying the vesical end of the plexus, is apt to cause necrosis.

7. Clinical experience confirms the results of anatomical studies and animal experimentation and shows that while many liberties may be taken with the ureter, the plexus should be guarded in all operations involving the ureter. The ureter has been freed for its entire length and yet necrosis has not occurred. Both internal iliac, the ovarian and the vessels of the round ligament have been tied with similar results. On the other hand, when the ureter is dissected free from some adherent mass, even for a short distance, as, for instance, from a carcinomatous cervix of the uterus, there is danger of necrosis, for the larger vessels of the plexus may not alone be destroyed, but also the smaller branches which are more intimately united to the ureter. In operations for cancer of the cervix this danger is increased where vessels supplying this portion of the ureter are ligated, as, the uterine, anterior branch of the internal iliac or the internal iliac artery. I cannot see that there is any operative advantage to be gained in ligating either the internal iliac or its anterior branch, over the ligation of the uterine alone, and there is this disadvantage that the chance of ureteral necrosis is not only increased but there is danger of lowered local resistance for the portion of the pelvis supplied by these vessels which would predispose these parts to infection.

8. Other accessory etiological factors must be considered in the causation of ureteral necrosis; as, infection, exudates, destruction of tissue about the ureter as would result from the use of a cautery, foreign bodies against the ureter (as gauze), pressure on the ureter, stricture of the ureter, and lowered general resistance. In addition, injury to the ureteral veins, although there is a free anastomosis between the veins in the wall of the ureter, must embarrass the ureteral circulation to a degree varying with the extent of the injury and so would interfere with the nutrition of the ureter.

9. Hysterectomy in carcinoma cervicis uteri, where the parametrium is removed mesial to the ureter, must leave cancer either in the form of metastases or as an extension of the growth into the parametrium in many cases. On the other hand, the chance for ureteral necrosis is slight, for the ureteral plexus surrounded by the pelvic ureteral sheath is uninjured.

10. The more radical operation with dissecting the ureter from its sheath offers a greater chance for cure than the above, but there is the danger of ureteral necrosis, for by freeing the ureter the vessels supplying that portion of the plexus are destroyed and the lower 3-4 cm. thus freed must be nourished by blood coming from the upper portion of the ureter through the periureteral plexus, and unless great care is taken this may be injured sufficiently to cause ureteral necrosis.

In addition, the ureteral sheath has been destroyed and that portion of the ureter becomes imbedded in scar-tissue, and its function is impaired with the danger of partial or complete ureteral obstruction, with the accompanying lowered renal resistance and liability to renal infection.

11. Resection of the lower 3-4 cm. of the ureters and the implantation of the renal end of the ureters into the bladder offers the greatest chance for a cure, and at the same time there should be less chance for ureteral necrosis, for the ureter above the parametrium can be brought down to the bladder with its plexus intact, surrounded by the pelvic ureteral sheath, and after implanting the ureter into the bladder its sheath may be sewed to the bladder and also the peritoneal flap in which this portion of the ureter with its sheath lies. The drawback to this procedure is the possibility of renal infection and stricture of the ureter from implanting the ureters under tension. The renal infection may possibly be controlled by the formation of a vesico-vaginal fistula and the freeing of the bladder and suturing the pelvic ureteral sheath with the peritoneal flap to the bladder should relieve the tension of the implantation.

12. Whichever course is followed in these operations, from the basis of anatomical studies and confirmed by animal experimentation and clinical experience, *the periureteral arterial plexus and also the ureteral sheath should be preserved.* As stated, this is in a measure met by resecting the lower portion of the ureters and implanting their renal ends into the bladder, as described above. This is the only operation justifiable where the growth has involved the ureteral sheath. On the other hand, in so-called favorable cases, one could free the tissue between the two pelvic walls and instead of resecting the ureters, the ureters with their sheath could be freed from an incision made through the parametrium lateral to the ureters, and thus all the tissue would be removed except the ureters and their sheath, and the dangers of ureteral necrosis and stricture would be reduced to a minimum. This plan looks well on paper, but the sheath is very adherent to the surrounding tissues and a careful dissection would prolong an already exhausting operation; and again, the chances of leaving minute metastases in the pelvis are greater than when the ureter is resected. For only by the use of the microscope can one with surety diagnose the presence of cancer in the parametrium. However, clinical experience alone can decide which method offers the greatest percentage of cures combined with the lowest primary mortality.

I am sure that many of us who are only too well acquainted with the mental and physical torture, the pain, the vesical and rectal fistulæ, etc., so generally associated with the clinical course of cancer of the cervix not operated upon, and the fact that such a large per cent recur after operation, which means that they have not escaped the above mentioned misery, will agree that any operation, no matter how severe, which gives the highest percentage of cures, is the one to be developed, not only in the advanced cases, but *especially in the early ones*, for in these there is the greater chance for a cure.

References.

1. Sampson: The Importance of a More Radical Operation in Carcinoma Cervicis Uteri, as Suggested by Pathological Findings in the Parametrium. Johns Hopkins Hospital Bulletin, 1902, XIII, 299-307.

2. Sampson: Ascending Renal Infection; with Special Reference to the Reflux of Urine from the Bladder into the Ureters as an Etiological Factor in its Causation and Maintenance. Johns Hopkins Hospital Bulletin, 1903, XIV, 334-352.

3. Quain: Quain's Anatomy. Longmans, Green & Co., London, 1896. Vol. III. Part IV. 205.

4. Morris: Surgical Diseases of the Kidney and Ureter. Cassell & Co., London, 1901. Vol. II, 284.

5. Disse: Von Bardeleben, Handbuch der Anatomie. Gustav Fischer, Jena, 1902, Band VII, Theil I, S. 110-111.

6. Margaroucci: Quoted by Monari and Protopopow.

7. Monari: Ueber Ureter-Anastomosen. Beiträge zur Klin. Chirurgie, 1896, XV, 722-723.

8. Protopopow: Beiträge zur Anatomie und Physiologie der Ureteren. Arch. f. die Gesam. Physiologie (Pflügers), 1897, LXVI, 21-22.

9. Kelly: Ligation of both Internal Iliac Arteries for Hemorrhage in Hysterectomy for Carcinoma Uteri. Johns Hopkins Hospital Bulletin, 1894, V, 53.

10. Pryor: The Surgical Anatomy of the Internal Iliac Artery in Woman and a More Radical Operation for Malignant Disease of the Uterus. Am. Jour. Obs., 1896, XXXIII, 801-817.

11. Pryor: Transperitoneal Simultaneous Ligation of Both Internal Iliac Arteries for Recurrence in the Cicatrix Following Vaginal Hysterectomy for Carcinoma Uteri. American Journal of Obstetrics, 1897, XXXV, 511-517.

12. Krönig: Die doppelseitege Unterbindung der Aa. hypogastrica und ovarica zur palliativen Behandlung des uterus carcinoma. Cent. f. Gyn., 1902, XXVI, 1073-1074.

13. Iwanow: Zur Kasuistik der Palliativebehandlung des uterus karzinoms durch Unterbindung der Becken gefässe. Berich über die geburtshilflich-gynäkologische Sektion des VIII Pirogowschen Kongresses russischer Ärzte in Moskau. Zent. f. Gyn., 1903, XXVII, 118-119.

14. Sänger: Ureteren chirurgie biem Weibe, medicinische Gesellschaft zu Leipzig, Nov., 1898. Reported in Münchener med. Wochenschrift, 1899, XLVI, 33.

15. Chrobak: Demonstration eines Falles von subserösem Uterus myom, Freilegung des Ureter. Geb. und Gyn. Gesellschaft in Wien, 1893. Reported in Cent. f. Gyn., 1893, XVII, 346.

16. Rühl: Ueber einer seltenen Fall von Ureterenverlauf bei Beckentumoren und dessen praktische Bedeutung. Cent. f. Gyn., 1898, XXII, 1056-1058.

17. Durante: Bolletino della R. Accademia medica di Roma. Anno XX, Vol. XV, 59. Ref. Boari, Anat. del Uretere, and Frommel, X, 351.

18. Wertheim: Ein neuer Beitrage zur Frage der Radikaloperation beim Uterus-krebs. Archiv für Gynækologie, 1902, LXV, 1-39.

19. Feitel: Zur arteriellen Gefäss versorgung des Ureters, insbesondere der Pars pelvina. Zeitschrift zur Geb. und Gyn., 1901, XLVI, 269-281.

20. Wertheim: Kurzer Bericht über eine 3. Serie von 30 Uterus krebs-operationen. Cent. f. Gyn., 1902, XXVI, 250-251.

21. Waldeyer: Ureter-scheide. Verhandlungen der Anatomischen Gesellschaft, 1892, 259-260.

22. Disse: L. C., S. 107 and 109.

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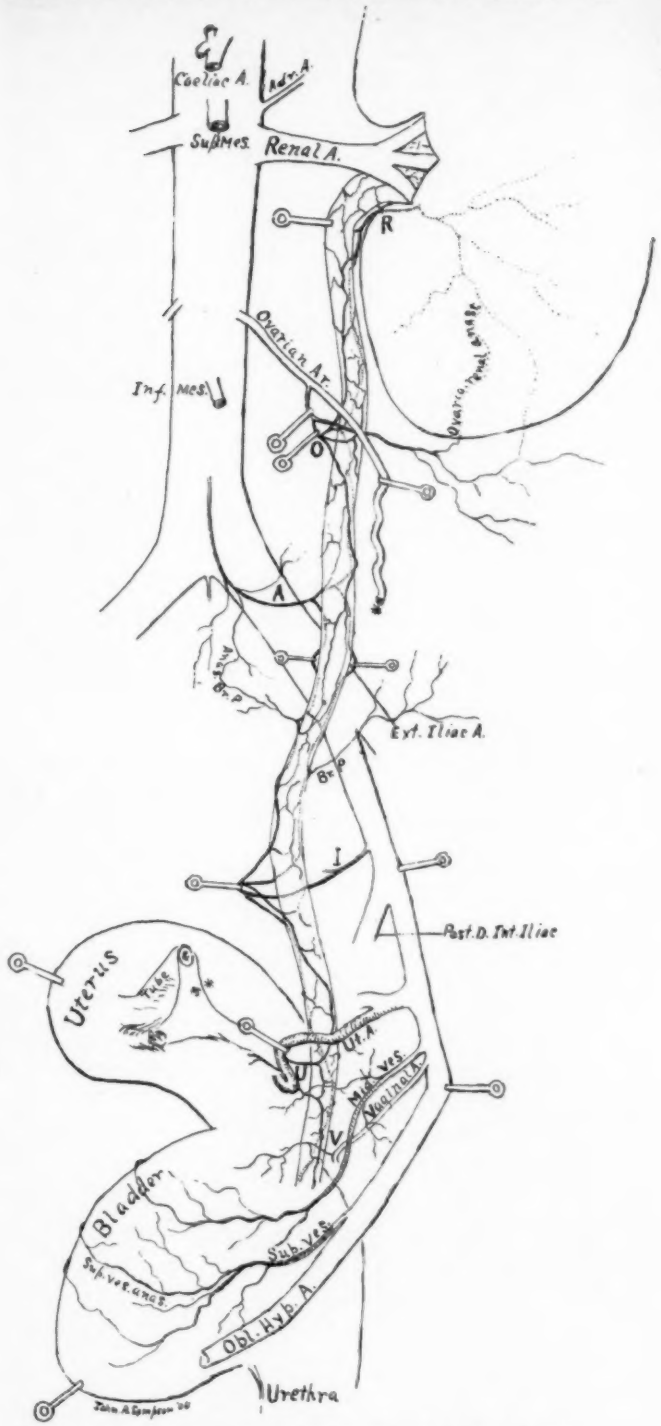

FIG. I.—THE PERIURETERAL ARTERIAL PLEXUS FROM A WOMAN 21 YEARS OLD, ×4/5. LEFT URETER.

The reft renal and right internal iliac arteries were injected with a 15 per cent solution of gelatine, colored with ultramarine blue. The organs were removed and hardened in 10 per cent formalin. The drawing was made from the dissected hardened specimen.

The periureteral arterial plexus in this instance is derived from branches of the aorta, renal, ovarian, internal iliac, uterine, and vaginal arteries, marked, A, R, O, I, U, and V.

Uterus drawn upwards and to the right, the tube and ovary have been removed.

Contracted bladder, drawn downwards and to the right.

Ovario-Renal Anast. Anastomosis between the subperitoneal branches of the uretero-subperitoneal arteries, arising from the renal and ovarian arteries.

* * Anastomosis between the uterine and ovarian arteries, cut away by the removal of the tube and ovary.

Br. P. Branch from the periureteral arterial plexus, supplying the tissue about the ureter.

Anast. Br. P. Anastomosis between the subperitoneal branch of the aortic uretero-subperitoneal artery, and a branch arising from the plexus.

Sup. Ves. Anast. Anastomosis of the superior vesical artery of one side with the superior vesical artery of the other side.

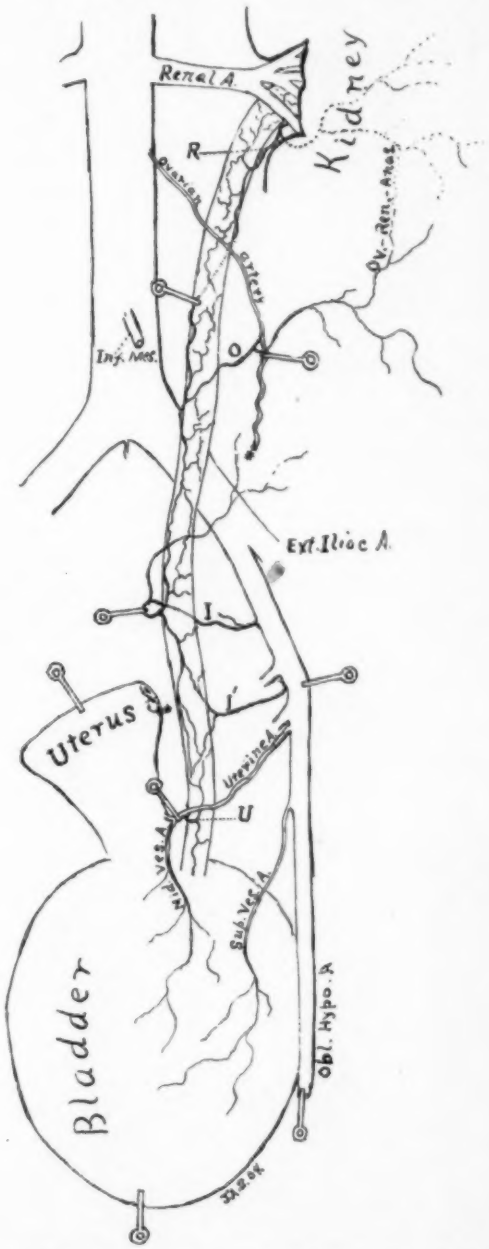

FIG. II.—THE PERIURETERAL ARTERIAL PLEXUS FROM A GIRL 7 YEARS OLD, ×1. LEFT URETER.

The left renal artery was injected with an aqueous solution of Prussian blue. The organs were removed and hardened in 10 per cent formalin. The drawing was made from the dissected hardened specimen.

The origin of the plexus differs slightly from that shown in Fig. I.

The aortic branch is absent, and the branch from the ovarian artery arises from that artery after it has crossed the ureter. There are two branches from the internal iliac artery and one from the uterine.

* * Utero-ovarian anastomosis, cut away by the removal of the tubes and ovaries.

Uterus drawn upwards and slightly to the right.

Distended bladder, drawn downwards.

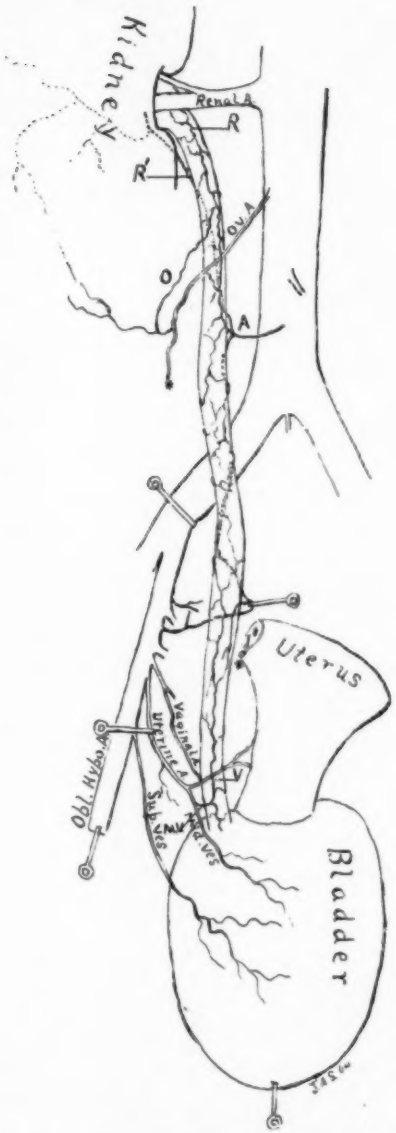

FIG. III.—THE PERIURETERAL ARTERIAL PLEXUS FROM A GIRL 3 YEARS OLD, ×1. RIGHT URETER.

Both renal arteries were injected with a 15 per cent solution of gelatine, colored with ultramarine blue. The organs were removed and hardened in 10 per cent formalin. The drawing was made from the dissected, hardened specimen. This represents another variation in the arteries giving rise to the periureteral arterial plexus. There are two branches, R and R′, from the renal, one from the aorta, A, one from the ovarian, which is recurrent, O, and has the form of an anastomosis of an artery derived from the plexus with a subperitoneal branch of the ovarian artery. The pelvic portion of the plexus is nourished by a branch, I, from the internal iliac, a branch M. V., from the middle vesical, which, in this instance, arises from the uterine also a branch, V, from the vaginal artery, which approaches the ureter from its posterior surface.

* * Utero-ovarian anastomosis.

Uterus drawn upwards and slightly to the left.

Bladder drawn downwards.

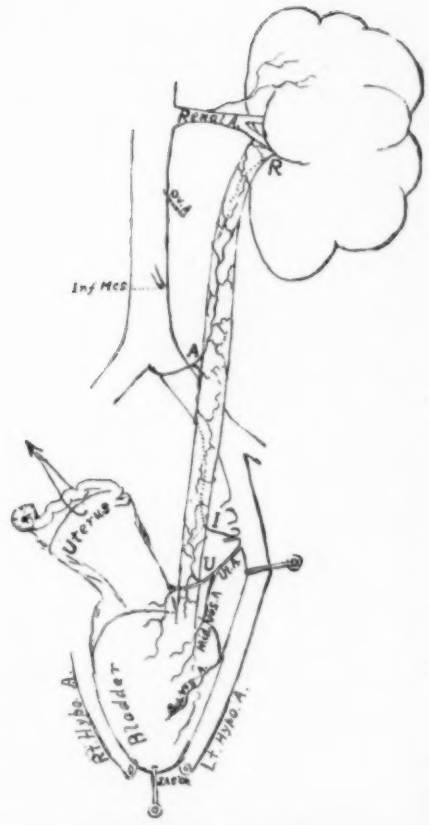

FIG. IV.—THE PERIURETERAL ARTERIAL PLEXUS FROM A NEWBORN GIRL, ×1. LEFT URETER.

The abdominal aorta was injected with an aqueous solution of Prussian blue. The organs were removed and hardened in 10 per cent formalin. The drawing was made from the dissected hardened specimen.

This again represents another variation in the origin of the periureteral arterial plexus. There is one branch, R, from the renal, the ovarian branch is not present, the other branches were derived from the aorta, A, internal iliac, I, and uterine, U, arteries. The uterus is drawn upwards and to the right.

These four illustrations represent four variations in the origin of the periureteral arterial plexus, which might be found in four adult specimens.

Compare the relation in size between the hypogastric artery and its branches in the infant and the adult, and the relatively greater size of the ovarian and uterine arteries in adult woman.

The ureter in this illustration has purposely been drawn, a trifle enlarged.

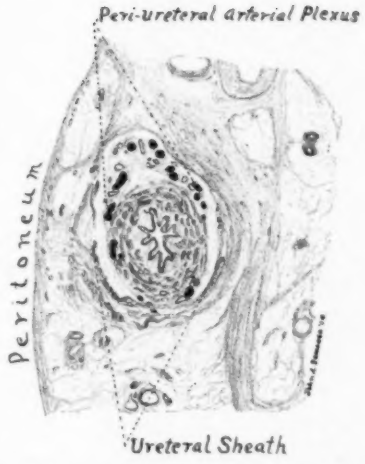

FIG. V.—CROSS SECTION OF URETER SHOWING THE PERIURETERAL ARTERIAL PLEXUS, AND THE URETERAL SHEATH, IN A WOMAN 21 YEARS OLD, ×5. RIGHT URETER.

The left renal and the right internal iliac arteries were injected with a 15 per cent solution of gelatine, colored with ultramarine blue. The organs were removed and hardened in 10 per cent formalin. The drawing was made from a cross section of the right ureter taken about 1.5 cm. above the uterus. Same case as one from which Fig. I was made.

For the sake of clearness only the ureteral arteries are drawn, as injected. The capillaries and the veins were not injected.

The periureteral arterial plexus situated within the ureteral sheath can be seen cut across, as well as small arteries within the ureter. This sheath of fibrous tissue which apparently is derived from the pelvic connective tissue, in this situation is adherent to the peritoneum and in freeing the peritoneum from the wall of the pelvis this portion of the ureteral sheath remains attached to the peritoneal flap thus formed This sheath serves as a protection to the ureter and its periureteral arterial plexus. See Fig. VI.

FIG. VI.—RELATION OF CARCINOMA CERVICIS UTERI TO THE URETER.

Transverse section of the parametrium and one-half of the cervix from a specimen of hysterectomy for carcinoma cervicis uteri in which the lower portion of the right ureter was sacrificed and the renal end of the ureter implanted into the bladder, ×2¼. Gyn. No. 10,494. Gyn. Path. No. 7515.

Section, right side, lower third of the parametrium. The carcinoma has extended out into the parametrium and has invaded the ureteral sheath thus causing it to hypertrophy and serve as a protection to the ureter from the growth, and later this progressive hypertrophy of the sheath will compress the ureter giving rise to a stricture and renal insufficiency.

The periureteral arterial plexus can be seen in transverse section, situated about the ureter within the sheath.

One can see that the growth does not have to extend far into the parametrium in order to reach the ureter.

TWO CASES OF LEUKOKERATOSIS BUCCALIS; COMPARISON WITH THE HISTOLOGICAL CHANGES IN A CASE OF TYLOSIS PALMÆ ET PLANTÆ.

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Dermatologists have been acquainted with disease of the skin, characterized principally by an increase in the horny layer for a much longer time than with similar disease of the mucous membrane. Consequently it is not surprising that the terms icthyosis (Hulke), tylosis (Hutchinson), keratosis (Kaposi), and psoriasis, applied to the former, have been used to describe the latter, since the clinical picture is so similar. Moreover, the disease was at first described by dermatologists and syphilographers and usually in connection with similar diseases of the skin. Alibert and Plumbe, in a case of icthyosis of the skin, describe similar whitish patches on the tongue.

Among the earliest reports on the disease as an idiopathic affection of the mucous membrane of the mouth are those of Müller in 1851 and Hulke in 1869. The latter described a case of white patches in the tongue as a case of "Icthyosis Glossæ," pointed out the pathological changes and noted the occurrence of epithelioma of the tongue six years after the removal of this patch. Schwimmer proposed the name leukoplakia for the disease. Perhaps leukokeratosis, used by Butlin, is a better descriptive name.

Leukokeratosis consists of more or less diffuse whitish, bluish-white, or pearly-grey colored patches, situated on the tongue or buccal mucous membrane. Schwimmer describes an earlier stage of the disease characterized by reddish areas in the mucous membrane. The duration of this stage is unknown.

We wish to describe a case in which the etiology is distinct, being clearly due to tobacco, another idiopathic case, and compare the histological changes present in these cases to a case of tylosis palmæ et plantæ, which it has been our good fortune to see. We wish to thank Prof. J. W. Lord for his kindness in allowing us to use the notes of this case, which was under his care in the wards of the Johns Hopkins Hospital. The illustrations of the sections are photomicrographs, taken by Dr. Chas. H. Potter, whom we thank heartily for his painstaking efforts in our behalf. Their clearness points out the great development that this branch has taken. It emphasizes the fact that we need no longer depend solely on drawings for illustrations of microscopical studies, which are so much better and accurately shown by photographs.

HISTORY OF CASES OF LEUKOKERATOSIS BUCCALIS.

CASE I.—Albert S., white, æt. 52, came to the Johns Hopkins Dispensary complaining of cough and hoarseness.

Family History.—Negative for consumption.

Patient's History.—Denies lues. For the last twenty years the patient has chewed tobacco and has made a practice of holding the quid of tobacco against the inside of the left cheek when not chewing.

Present Illness.—Began with a slight cough in the winter of 1901. Some difficulty in swallowing 6 weeks ago. Caught cold one week ago while in a perspiration.

Physical Examination.—In the left cheek, where the patient has held his tobacco, is an irregular greyish-white patch about the size of a half-dollar, slightly raised above the level of the surrounding mucous membrane. A small piece of this tissue was excised for examination.

The mucous membrane of the nose and pharynx was atrophic. There was a slight injection of the vocal cords and interarytenoid area. The patient was seen some weeks later when the place excised was covered by fine greyish-white plaques like the rest of the patch.

The tissue was fixed in formalin and sections stained with thionin, Van Gieson's stain and hæmatoxylin and eosin.

HISTORY OF SECOND CASE.

S. K., black, about 30 years of age. Complained of spitting blood.

Family History.—Negative.

Personal History.—Denies lues of which he gives no history of secondary lesions. Moderate smoker and drinker but used to drink heavily.

Present Illness.—Few days ago expectorated blood. The patch of leukokeratosis gave him no trouble.

Physical Examination.—Nose, pharynx and larynx normal. Chest, normal. On the roof of the hard palate, extending into the soft palate, is an irregular patch, slightly elevated, in places silvery white, in places deeply pigmented. Feels hard to the touch.

A small piece of this was excised.

HISTORY OF A CASE OF TYLOSIS PALMÆ ET PLANTÆ.

The patient, S. W., black, æt. 20, entered Prof. Osler's wards of the Johns Hopkins Hospital October 31, 1898, complaining of pain in the feet.

Family History.—Negative; none of his family had a similar trouble.

Patient's History.—Has had measles and whooping-cough. Denies gonorrhœa and syphilis. Moderate drinker and smoker. He has been healthy except for his present trouble,

which, he says, has prevented him from ever doing a whole day's work.

Present Illness.—Ever since the patient can remember he has had callosities on his hands, feet and anus. He says that he has heard people say that they began to appear as soon as he began to walk. He first noticed a row of corns on the palms of each hand and several little white places on his soles. They gradually got worse, assuming the present state in his hands, six to seven years ago. On the soles, the left has remained about the same for the past six to seven years, but during the past three to four months, the right sole has become much worse, having been about the same as the left up to this time. He says he had a similar spot over the left wrist, which he used to pare down continually with his knife, just as he does the other places now. This spot has gradually disappeared. No other growths have disappeared.

There is a constant ache in the horny hard areas. His feet pain him considerably when he walks. There is no itching.

Physical Examination.—The patient is a well-nourished, fairly good-sized, black-skinned negro. There is marked glandular enlargement. Soft systolic murmur heard after the first sound at the apex of heart, faintly heard in the axilla and over the body and base of the heart.

Both knee-jerks are somewhat exaggerated.

The distribution of the lesion of which the patient complains is on the palms of both hands, soles of both feet, over the sacrum, and about the anus. On the palms, extending from the wrist on the ulnar side, to the little- and ring-fingers, is an area about half an inch in width in which the skin is elevated. This patch merges into a similar patch about the metacarpo-phalangeal joints of the fingers, which extend half way down the ring- and middle-fingers. There is also an irregular patch on the thumb and between the thumb and index-finger. The lesions are exactly symmetrical on the palms, as can be seen from the photographs (Fig. 1), which show very well the distribution and character of the lesions. In these areas the skin is somewhat elevated, of a yellowish-white, translucent color and can be readily peeled from the underlying part without causing the patient any pain.

On the soles the distribution is not so symmetrical. On the left sole, the lesions occur in patches; on the inner aspect of the heel is a round patch two inches in diameter, on the middle of the foot is a half-dollar sized patch, over the fifth and second metatarsal bones are two quarter-sized patches. In all these places the skin is raised, hard, greyish-white and somewhat translucent. On the right soles the picture is different. The whole of the heel and outer side of the sole is involved; also the proximal part of the great toe and the distal part of the third and fourth toes. Over the heel is a dollar-sized excavated space, the walls of which are much raised and cornified. There is also a long depression, four by three-quarters inches on the outer side of the sole, the base of which is of a greyish-white color, somewhat sodden, of horny consistence and somewhat tender to the touch. The walls of this depression consist of a wide area of the thickened skin, possessing the characteristics of that before described. At the heel on the right sole and slightly ventral to it the disease is seen and felt to be advancing up the heel for about two inches. Here the skin is harsh, thickened, of a blackish color and hangs down in small folds in places.

There is excessive sweating in the affected areas. In other parts of the body the skin is very dry and cutis anserina is well marked. There is no disturbance of sensation for touch, pain and temperature sense. The affected areas pain him a good deal but do not itch.

Owing to the extent and situation of the lesions in the hand there is marked deformity. The ring- and little-fingers are drawn up as in Dupuytren's contraction and the first phalanx of the thumb is held in an adducted position. The appearance of abduction of the terminal phalanx of the thumb, as seen in the photograph, is not real but is due to the effort to abduct the whole thumb. There is no deformity of the feet.

Besides the lesions on the palms and soles, there are other (similar) lesions on the coccyx and about the anus. Over the coccyx is an irregular, horny projection about the size of a half-dollar, of a yellowish-brown color. Projecting from the right side of the anus is a mass about the size of a hickory-nut, exhaling a peculiar, disagreeable odor. The surface of the mass is, for the most part, of a pinkish-red color. The part nearest the skin is of a yellowish-white color and this blends finally with the normal skin. Just below the the trochanters are two half-dollar sized areas of thickened black skin. The mass about the rectum was excised and the diagnosis of the tissue was epithelial hyperplasia, non-malignant. On the day of admission a small piece of skin was removed from the inner side of the foot, right above the heel. This was fixed in ten per cent formalin and sections were stained with hæmatoxylin and eosin and Van Gieson's stain.

Microscopical Appearances in the Cases of Leukokeratosis Buccalis.

Case I.—The most striking thing about the section, which is extremely well shown by the photomicrograph (Fig. 2), is the extreme thickness of both mucous membrane and submucosa. Secondly, there is present as a new layer, a very thick, horny layer, just as in the skin but much thicker.

The mucous membrane of the patch consists, then, of two distinct layers, an outer horny layer, staining well in eosin, and an inner layer, Malpighian layer, staining well with hæmatoxylin.

On high magnification very indistinct cell-outlines are seen in the outer horny layer but there is no nuclear stain.

The Malpighian layer is much thickened, most of the cells are typical polygonal prickle-cells with well-defined nucleus and nucleolus. Farther out near the horny layer the cell-outline as well as nucleus becomes indistinct. Instead of a well-defined nucleus one sees numerous small, black granules scattered through the cell. An occasional polymorphonuclear leucocyte is seen between the lowest layers of cells. The

papillæ have disappeared in great part, but in places very narrow extensions of the submucosa run up into the Malpighian layer. Also in the lower part of this layer are cross-sections of the papillæ. The Malpighian layer is sharply marked off from the submucosa.

The submucosa is very strongly infiltrated with young, round cells which are especially abundant just beneath the Malpighian layer and about the blood-vessels. There is a great deal of proliferation of the connective tissue of the submucosa, shown by the great number of embryonal cells present. There are numerous blood capillaries amongst this tissue which looks as if it is newly formed.

These points are brought out well by Van Gieson's stain, which also accentuates the difference between the inner layer of the Malpighian cells and the outer layer of second rows of cells which are filled with granules.

CASE II.—This is practically a reproduction of the changes described in Case I, only all the layers are much thinner. The plaque in this case was not elevated as much above the surface as in Case I. It also differs in that the granular layer, or layer of cells filled with black granules next the horny layer, stands out very distinctly, while it was indistinct in Case I. See Fig. 3.

MICROSCOPICAL APPEARANCES IN THE CASE OF TYLOSIS PALMÆ ET PLANTÆ.

The photomicrograph, Fig. 4, shows very well the great thickness of the epithelium. This section was taken from a part just above the developed spot of the disease. In certain parts, as the heels, slices of horny epithelium one-eighth of an inch thick could be shaved off. The epidermis presents a remarkable appearance, due to the number and arrangement of the layers, which can very well be made out with the low magnification.

Beginning from within, we have the following lesions:

1. Stratum mucosum. Somewhat thickened. Cross-section of papillæ seen in the lower parts of the layer.

2. Stratum granulosum. Three to four layers of cells at outer part of stratum mucosum, showing as a faint blackish line in the photomicrograph. The nucleus is round and distinct, stains intensely with hæmatoxylin, the cells contain blackish granules.

3. A thin area staining a homogeneous pink, and outside of this is a thick band of bladder-like cells. This layer appears as a thick, white band in the photomicrograph.

4. A layer of cells closely packed together with long, thin nuclei staining intensely with hæmatoxylin and cell-bodies staining red with eosin. This shows as a rather thick, black space in the photograph.

5. A thick, reticulated layer staining a faint pink with eosin. The inner two-thirds of this has the appearance of large, long, bladder-like cells, like in layer three; the outer third is composed of homogeneous pink-staining strands.

The papillæ are very numerous and extend rather deep into the mucous layer. Small blood-vessels are rather numerous in the stratum papillare. About some of these are a few young round cells. There is a slight amount of young embryonal tissue in this layer. There is nothing of especial note in the stratum reticulare.

The essential changes in both these diseases are very much alike, namely, first, the process of keratinization resulting in one case in the formation of a new layer, and in the other a great increase in the thickness of the horny layer, and secondly, the infiltration of the corium and submucosa with young round cells. In the cases of leukoplakia this is more marked and the tissue has a more embryonal appearance. The tylosis case was of longer duration and the tissue presented a more organized state of connective tissue.

The difference in the size of the papillæ is perhaps explained partly by the location. Normally the papillæ in the mucous membrane of the buccal cavity are not very well marked, while they are very well marked in the feet.

It is interesting to note that Leloir states that in cases of leukoplakia lingualis complicated by epithelioma, the layer of granular cells stops where the epithelioma begins.

Leukokeratosis buccalis is found on the tongue, inside of cheek opposite where the teeth meet and rub it, rarely on the hard palate, uvula, gums and lips. Schwimmer saw but twenty cases in twenty-thousand cases observed in nine years. Nedopil stated its rarity in the clinic and private practice of Billroth. In the throat department of the Johns Hopkins Hospital Dispensary there have been seen but two cases in the last three years.

The disease occurs between the twentieth and sixtieth years of age, almost always in men. Among twenty-five cases seen by Débove there was not one woman.

The course of the disease is variable. It may remain unchanged for years, the patches merely becoming thicker and thicker. In Hulke's case the patient was in the habit of paring off the superficial layers from time to time. It tends to recur if removed "en masse." The superficial layers may peel off spontaneously, leaving reddened areas. The papillæ on the tongue atrophy, leaving a smooth thickened area. The most serious sequela is the development of carcinoma; this developed in four of Schwimmer's twenty cases. Morris, in a study of the relationship between this disease and carcinoma of the tongue, says that of twenty-five cases of early tongue carcinoma, ten were preceded by icthyosis, usually very diffuse.

Etiology.—It is probable that the mucous membrane of persons developing this disease is peculiarly susceptible, just as the skin of certain individuals is delicate and prone to the development of certain skin diseases. In such people any strong irritation will start the disease. Such an irritation is the use of tobacco, chewed or smoked. Smokers' patches begin usually on the tongue, where the stem of the pipe rests, or where the smoke from the cigar, cigarette or pipe impinges on the mucous membrane, as small reddish spots. In one of our cases the spot developed exactly where the patient was in the habit of holding his quid of tobacco. These patches are covered, after a while, by a yellowish-white or brown material

which becomes detached to make place for a fresh covering. The patch tends to spread over the tongue and cheek, and, in time, may turn to a bluish-white or grey-white patch. Alcohol, condiments, very hot and irritating foods and syphilis are potent predisposing causes. The majority of Morris's cases had syphilis and were drinkers and smokers. Schwimmer claims that they can be produced by the action of mercury alone. He says that workers in mercury mines, mirror- and barometer-makers, suffer from inflammation of the mucous membrane of the mouth, with swelling and the formation of ulcers, and also show whitish or bluish-white patches in different parts of the mouth. He has seen luetic cases grow worse under mercurial treatment. Butlin has seen leucomatous areas develop along the line of vulcanite tooth-plates. He also thinks that gout and rheumatism play a part, especially in young people. The French writers lay great stress on these two diseases as etiological factors. Schwimmer found a number of cases coexistent with catarrh of the stomach and intestines, and improvement of the patches occurred with improvement of these diseases.

Symptoms.—Very often, as in our cases, there are no symptoms and the patient only accidentally becomes aware of its presence. There may be a slight dryness and hoarseness, or the sensation of burning in eating, especially highly-spiced food. There is no actual pain. When extensive and thick patches are present, difficulty is experienced in moving the parts. Often the patient complains of great thirst. Taste is unaffected unless the patches are very extensive.

Diagnosis.—In a well-developed case there is no doubt as to the diagnosis. The coloring and extent of the patch, its persistence and hard, elevated surface are enough to establish the diagnosis beyond any doubt. Luetic patches develop quicker and there is enlargement of the neighboring lymph-glands. These patches also tend to disappear, which is rarely the case with leukokeratosis. Spots in the mouth in lichen ruber planus and pemphigus occur with the general skin diseases. Their origin, arrangement and tendency to disappear should differentiate them.

Prognosis.—Recovery is possible when the patches are not so extensive and are soft and pliable. Butlin says, however, that he has never seen a well-developed case recover. The possibility of development of carcinoma in these cases must be thought of and the patient warned of the danger of the malady becoming serious if not attended to.

Treatment.—All sources of irritation should be removed. The use of alcohol and tobacco should be discontinued and the patient avoid very warm and spicy foods and drinks. Rough teeth and badly-fitted plates should be attended to. Constitutional treatment should be carried out in cases of rheumatism, gout, gastric or intestinal disorders. However, in cases of some standing following syphilis, antisyphilitic treatment is of no value, as the use of mercury may aggravate the lesion.

In the milder cases much can be done by the use of alkaline mouth-washes, such as bicarbonate of potash, thirty grains to an ounce of water, chlorate of potash, peroxid of hydrogen. Chromic acid, ten grains to the ounce, is often of use, especially in the cases following syphilis.

When there is quite a thickening of the epithelium, salicylic acid in alcohol (Ac. Salicylic 0.5 to 1, Spts. vini rectificat., aquæ destillat. aa. 10.0), painted on the affected spot every alternate day is of great value. Leloir claims this is good on account of the dekeratinizing action that salicylic acid possesses. A mouth-wash of alum, two grains to the ounce, is of use. If there is an acute inflammation on top of the usual conditions, a mixture of honey and borax may be painted on it.

The use of an ointment on the part as suggested by Butlin is very valuable, especially to be rubbed in at bed-time to keep the part from becoming dry and cracking. Such an ointment may be made of six drachms of lanolin and two drachms of vaselin as a base, with any drug desired, such as boric acid. The use of caustics is to be advised against, as the general consensus of opinion is that they increase the irritation and increase the predisposition to the development of carcinoma.

If the patch is very thick and circumscribed it may be excised. Hulke excised the patch in his case but it had returned on a second observation three years later. Lawrence operated on his case, shaving off the growth with a scalpel. As in Hulke's case, this was followed by profuse hæmorrhage. Lawrence saw his patient seven months after the operation, when the former disease had returned but increased in size. It was again removed.

Ranschoff reports two cases operated on, one well for two years, another for five years after the operation, no scar being left.

Bibliography.

Butlin, H. T.: Medico-Chirurgical Transactions of London, Vol. LXI, p. 51.

Butlin, H. T.: Diseases of the Tongue, London, 1900.

Friedrich: Rhin., Laryng. and Otology in General Medicine.

Lawrence: The Lancet, May, 1862, p: 459 and January, 1863, p. 93.

Leloir, H.: Archives de Physiologie, 1887.

Morris, H.: The Lancet, 1882, Vol. I, p. 776.

Morrow, P. A.: Medical News, 1886, p. 295.

Plumbe, S.: Diseases of the Skin, 1837, p. 311.

Ranschoff, J.: Annals of Surgery, 1899, p. 577.

Rosenberg: Die Krankheiten der Mundhohle, des Rachens. und der Kehlkopfes, Berlin, 1899, S. 39.

Schwimmer, E.: Vierteljahrschrift f. Dermatologie und Syphilis, 1877, S. 510.

Zeigler: Special Pathological Anatomy.

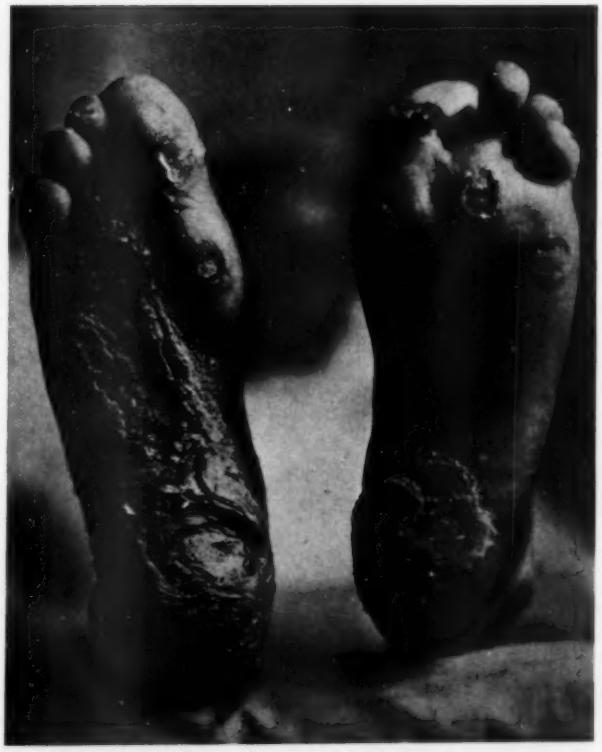

FIG. 1.—Photograph of palms and soles of case of tylosis palmae et plantae.

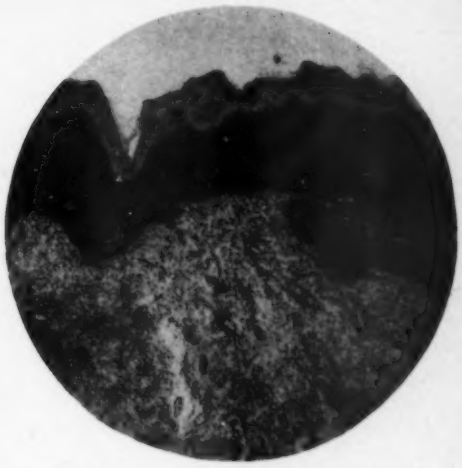

FIG. 2.—Photomicrograph of first case of leukokeratosis buccalis. Dr. Charles H. Potter. ×25.

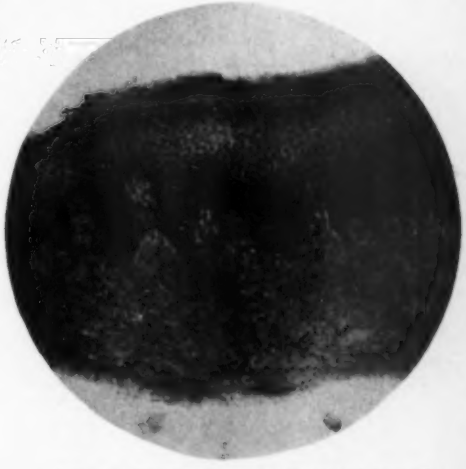

FIG. 3.—Photomicrograph of second case of leukokeratosis buccalis. Dr. Charles H. Potter. ×25.

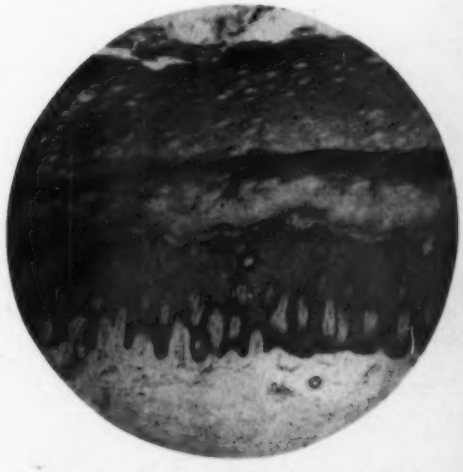

FIG. 4.—Photomicrograph of case of tylosis palmae et plantae. Dr. Charles H. Potter. ×25. Zeiss's planar lenses and Cramer's isochromatic plates.

THE EFFECTS OF X-RAYS UPON LOWER ANIMAL LIFE AND THE TUBE BEST SUITED TO THEIR DESTRUCTION.[1]

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I. The immediate object of this research was to ascertain what effects, if any, X-rays have upon several of the lower forms of animal life; to discover if any of such organisms are destroyed by X-rays and if so, what technique best produces such destruction.

II. The reason for such research is based upon the analogy existing between such lower organisms and the new cells of a malignant growth. What I really wish to establish is a scientific method by which to determine the best form of tube with which to treat such growths; and it seems but fair to allow, upon such analogy, the supposition that the condition of tube that is most destructive to one of these forms will be most destructive to the other.

This does not mean that the most destructive form or arrangement of tubes will be the best for the treatment of epitheliomatous or sarcomatous conditions, for therapeutically you must consider also the effects upon healthy tissue, upon the nerves, the circulation, etc. It simply means that one may have found the first step in considering such treatment, that is, the destruction of the malignant cells. The organisms I chose for my experiments were: *Chilomonas, Paramoecium aurelia, Paramoecium bursaria, Cryptomonas, Rotifera, Arcella.*

III. The only other account of research work along the same line that I have been able to find was that published in Berlin, in 1899, in the Archiv für die gesammte Physiologie des Menschen und der Thiere, by Dr. F. Schaudinn. But Schaudinn's work differs from mine in two important particulars. He is concerned about the number and nature of the lower organisms affected by X-rays and how they were affected; I about the tube and conditions best effecting the destruction of any of them.

Again, his technique, his apparatus and the time given to experiments differed from mine. The modern improvements along these lines permit of my reducing to minutes the fourteen hours he exposed his specimens to the light. The organisms which he found to be destroyed were: *Amoeba princeps* 25 per cent died, *Amoeba lucida,* all died, *Pelomyxa palustris,* all died, *Gromia oviformis,* died, *Actinosphaerium eichhorni,* died, *Chilomonas paramoecium,* died, *Cryptomonas ovata,* died, *Euglena acus,* died, *Oxyrrhis marina,* died, *Spirostomum ambiguum* died. *Cryptomonas* was not destroyed in my experiments. Otherwise these reports mutually prove one another.

IV. I spoke of the difference in technique employed by Schaudinn and myself. It is in regard to the technique that I find the greatest care necessary. Perhaps the points to be most insisted upon are the use of control specimens; the selection of the best rays of the light, as well as the best distance between the tube and the specimen; and the proper method, number and times of exposure. As to control specimens, every possible attention has been paid to them throughout my experiments. Never have I exposed a specimen to the rays, without placing another specimen, as nearly similar to the first as possible, in a lead box safe from the rays. When a specimen has been exposed to the sunlight for microscopical examination, its control has been placed as nearly as possible in the same light even to the condenser where a condenser has been used. In shallow water the specimens are very susceptible to strong sunlight.

There is quite a difference to be noted in the different rays. The strongest are those directed from the centre of the anode plate in a line perpendicular to its face. I also soon discovered that the best results are obtained if a sheet of lead be rolled into a cylinder and the rays directed through this. I considered this focus tube and the proper direction of the rays of great importance. The most destructive rays were produced by a medium low tube excited by a heavy electrical discharge which had been passed across spark-gaps or through other resistance sufficient to produce rays of great penetrative power. Such a tube would give a clear picture of the hip of a man weighing 170 pounds in three and one-half minutes. Very low tubes which show no bones, but only the outline of the hand upon the fluoroscope have shown no effect upon the organisms, nor have the ultra-violet tubes influenced them. Very high tubes which were not heated by the heaviest discharges of my apparatus after ten minutes of exposure, gave very poor results. I used an 18-inch coil.

We have now seen how to get the best rays; I find the distance such rays must travel from the tube to the specimen to be also a matter of great importance. Regarding this, several important conditions must be considered. It is a well-known fact that a high potential current passing through a partial vacuum tube induces a secondary current upon the outside of that tube. This is the principle upon which high-frequency tubes are operated. The high-frequency discharge is in some way very destructive to these organisms if brought into too close relationship with the specimen. The destructive effect may be due to the liberation of ozone, a great deal of which is produced; or it may be due to some form of elective discharge direct. A Crook's tube is a partial vacuum and has passing

[1] Read before the American Roentgen Ray Society, December 10, 1903.

through it a high potential current, and, therefore, has an induced or high-frequency current upon its outer surface, though this induced current is not nearly so strong as that produced by the high-frequency apparatus. In all experimental work it is necessary to make the tests as simple as possible. I have tried therefore to eliminate the possibility of this induced current affecting my experiments. The high-frequency current which is, as I have said, a much stronger induced current than that from the X-rays, had no effect upon the specimen when removed from it five inches. For this reason the distance of my X-ray tube from the specimen has never been less than five inches. I soon found that the closer the tube the more potent the rays. As five inches was considered the closest I dared to bring the tube in absolute safety, I early adopted five inches as the standard distance.

We have spoken of the most destructive rays and the standard distance, let us now consider the exposure of the specimen under these conditions. My method of exposure has been to take a small, thin rectangular frame of brass, such as fits easily upon the ordinary microscopic slide, a counting cell in fact, of the Sedwick-Rafter type as modified by Calkins, Jackson and Whippler. This brass rim is cemented to a glass slide and the cell is 50 mm. long, 20 mm. wide, and 1 mm. deep. The superficial area thus is 1000 sq. mm. and contents 1 cc. This is used for the microscopical quantitative examination of water. As can be seen, this presents to the rays a very broad surface with little depth. It is easily examined under a low-power microscope without a cover-glass. The greatest difficulty is found in keeping sufficient water over the organism. Evaporation is very rapid. This was obviated by having a small cup of water with a piece of absorbent cotton twisted into a wick to extend from the cup to the receptacle on the slide. The slide is placed lower than the surface of the water in the cup and the water is thus gradually drawn to the slide. If the water in the cup is much higher than the slide, the slide will be flooded. The control must be arranged with similar care. The number of exposures varied from three to fifteen. The duration of each exposure was from three to twenty-one minutes. The time allowed between exposures was at first twenty-four hours, later only one hour. When the duration of each exposure was longer than I cared to use my tubes, I allowed an interval of five minutes after each exposure of three minutes. I think that this covers the matter of the technique used throughout the experiments. Perhaps it would be well to take a typical experiment and follow it through, since time will not permit a detailed account of all of those from which my facts have been drawn. I choose one in which any deviation of the technique would give markedly poorer results.

V. Apparatus: Coil 18 inches—mercury turbine interrupted drawing 5½ amperes from a 64-volt storage battery—2 spark-gaps of 3 inches each, 2 vacuum tubes, one high, the other low, in series with a medium low Gundlach tube of 8-inch diameter. The same apparatus worked in a similar manner has taken a good hip picture for me in three and a half minutes. The specimens to be treated were arranged on a slide and controlled as I have previously described. The tube was focused through the lead cylinder, from the center of the anode, with the face of the tube five inches from the slide Upon the slide were:

1—*Chilomonas.*
2—*Paramoecium aurelia.*
3—*Paramoecium bursaria.*
4—*Cryptomonas.*
5—*Rotifera.*
6—*Arcella.*

The extract from my notes reads:

Date	Interval	Exposure	Time	Specimens	Control
Nov. 10	.....	First	3 min.	No change.	No change.
" "	1 hr. later	Second	" "	" "	" "
" "	2 hrs. later	Third	" "	A little stiff.	" "
" 11	.....	Fourth	" "	1 and 2 no mobility; the rest seem sluggish.	" "
" 11	1 hr. later	Fifth	" "	1, 2 and 3 no mobility; 4, 5, 6 possibly sluggish.	" "
" 12	.....	Sixth	" "	1, 2 and 3 dead; 4, 5 and 6 no change.	" "
" 13	.....	Examination		1, 2 and 3, dead; 2 fatty degeneration with high power; 4, 5, 6 no change.	" "
" 15	.....	Examination		1, 2, 3 not seen; 4, 5, 6 no change.	" "

This is an example of research experiments which have been verified by me many times, and I consider that it shows the best method of obtaining the most decided reaction. With higher or lower tubes, with a greater distance between the specimen and the tube, focused differently, or focused without the lead cylinder, the results are less marked, or the necessary time of exposure is longer.

As a general law, living tissue is stimulated when subjected to a properly attenuated destructive force. If this was so with regard to the effect of the X-ray upon the specimens, I failed to note it; but I consider that further work along this line may prove that a tube properly focused, with the current exciting the tube to the proper rays, may produce increased activity among these organisms. But I have failed to note any such result.

Another deduction made from these experiments is that they who claim that the cathode rays and not the X-rays are essential to the destruction of epithelioma are probably wrong. The same tube when excited by a greatly resisted current is much more destructive than when excited by a current of lower potential. The amount of the X-ray in the latter case is practically nothing when compared with the former. In the case of the current of lower potential too, the cathode rays appear to the eye much greater. Therefore, I believe the destruction is due to the X-ray.

VI. Having discussed the technique most effective in these experiments; given an illustration of a typical experiment; and drawn from it such deductions and observations as are best substantiated by all my work, I feel that we are now able to answer the questions asked at the beginning of the research.

First, what effect has the X-ray upon lower organisms? We have seen that some of these organisms are killed by the X-rays, while others are apparently unaffected by it. The *Chilomonas, Paramoecium aurelia* and *Paramoecium bursaria,* all forms of single cell-life belong to the first class, while *Rotifers, Arcella* and *Cryptomonas* were unaffected by the light. *Chilomonas* were the most numerous and showed the first effect of the rays, and after being destroyed, gave decided evidence, under the high power, of fatty degeneration. The Paramoecia were markedly affected but were not nearly so numerous. I noted no fatty degeneration in these specimens, but this was possibly due to lack of sufficient effort. In speaking of the effect of X-rays upon these organisms, we must note again that there was no stimulation prior to death.

The second question asked was: "can any of these lower organisms be destroyed by the X-ray?" This question is almost answered in the first, but it is important to note here that through the use of controls and care in technique we have eliminated as the destructive force any other agency than the X-ray; the most possible of such other agencies being the sunlight, an induced electric current and the cathode rays.

Question three—"what technique best produces such destruction"—has been answered in detail throughout this paper. Should we confine our question to the use of tubes, we can sum up our deductions in three statements. First, the closer the tube to the object treated the more destructive the rays. Second, lower tubes excited by small currents are not so destructive as lower tubes excited by heavier currents, which are resisted. And third, very high tubes have very little effect.

VII. We have now reached our real conclusion. Since we have established what technique best produces destruction of certain lower cells by X-rays and have acknowledged the analogy existing between these lower organisms and new malignant cells we have decided (bearing in mind that the possibility of destroying healthy tissue is to be eliminated) that the best rays to destroy epitheliomatous and sarcomatous cells is the lower tube excited by a heavy current with much resistance.

Thus perhaps our first step towards the cure of these malignant growths has been taken.

AN ANOPHELES MOSQUITO WHICH DOES NOT TRANSMIT MALARIA.

BY LEONARD K. HIRSHBERG, A.B., M.D.

(From the Pathological Laboratory of the College of Physicians and Surgeons.)

Anopheles punctipennis abounds in the neighborhood of Roland Park, a suburb of Baltimore, as was demonstrated by us[1] some time ago. Even at that time, in a careful investigation of the health records and specimens sent to Dr. William R. Stokes, City Bacteriologist, I was unable to trace any autochthonous cases of malaria in that neighborhood. After carefully searching through much of the literature[2] on mosquitoes and malaria, and not finding any malaria traceable to *A. punctipennis* as carriers of the parasite, it was determined last summer to put the question to a proof.

The few cases of malaria which occur in Baltimore have their origin as a rule at Sparrow's Point and upon the Eastern Shore of Maryland. At the former place, situated some twelve miles from the city, we found *Anopheles maculipennis* in abundance, but found no other species of Anopheles in numbers. Malaria is constantly endemic there and most of the Baltimore cases are imported from that place. *Anopheles maculipennis* captured there contained malarial parasites in the stomach walls. On the other hand, I have never been able to demonstrate the parasites in the walls of *A. punctipennis* found at Roland Park or elsewhere.

The coincidence of malaria and *Anopheles maculipennis* holds better in Grassi's[3] investigation of the geographical distribution of malaria and mosquitoes than in the case of *Anopheles punctipennis.*

The differences between these two species of Anopheles are now so well known, and can be so easily found in the literature[3] that I shall not stop to consider them. In collecting the larvæ, the method suggested by G. H. F. Nuttall[4] was carried out.

Larvæ of *Anopheles punctipennis* were collected from streams in the grounds of the Baltimore Country Club at Roland Park and measured from 2.4 mm. to 8.1 mm. in length. About the same time, in order to have controls, larvæ of *Anopheles maculipennis* were obtained from the inlets about Sparrow's Point. Most of these larvæ, owing to the cool weather, did not metamorphose into pupæ until from fourteen to eighteen days. They were fed upon spirogyra and algæ of various kinds.

The imagoes developed from the pupæ in from two to five days. The imagoes were fed upon fresh fruits, juices, preserves and sugar water, kept constantly in the mosquito cages.

When an available case of malarial infection presented itself, the following method[4] was carefully explained to the patient and his consent and co-operation obtained. The lobe of the ear or the extensor surface of the hand was carefully cleaned some time before the mosquitoes were brought in contact with the patient. This was done because the female mosquitoes would not bite the skin which had been freshly

cleaned with various solutions such as soap, ether, alcohol and bichloride.

An adult female *A. punctipennis* and an *A. maculipennis* were then placed in separate test-tubes plugged with cotton and covered with black paper. It was found that the mosquitoes would bite more quickly in this way, than if the tubes were held under the cover-slips. The act of biting could also be better observed through the small part of the tube near its mouth, which was not covered.

Patients suffering with estivo-autumnal malaria showing crescents in the peripheral circulation were the only ones considered available.

After one female adult of each species had bitten the patient and become quite swollen with the blood they were each taken away and incubated at a temperature of 30° C., as described by Bignami and Ross.[7] The mosquito was then anæsthetized by ether and fixed upon a piece of colored glass by a needle passed through the thorax. If a needle is lightly pressed at the third abdominal segment and drawn apart from the other one by gentle traction, the entire intestine is withdrawn. This is best done in a normal saline solution. The salivary glands are obtained for examination by fixing the thorax and detaching the head lightly with a needle, when, as a rule, the tubes and ducts become visible. At times it becomes necessary to take away a segment of the thorax. Marchiafava and Bignami[8] have described this procedure in detail.

After the infected mosquitoes have been incubated at 30° C. for periods varying from forty-eight hours to seven days, the intestinal wall in the successfully inoculated Anopheles showed in the early stages the zygotes with the peripherally arranged pigment. The mosquitoes dissected after the third day showed little pigment in the parasites, but indicated a well-determined capsule. Later stages again demonstrated the nucleated hyaline cystic bodies and the filamented sporozoites. The salivary glands contained parasites (sporozoites) only after the eighth day.

In forty-eight attempts to inoculate the *Anopheles punctipennis* from five cases of estivo-autumnal malaria in which crescents were easily and constantly demonstrated in the blood, there was absolutely no evidence of the parasites in the stomach walls, intestines, body cavity or salivary glands after the most minute search. At the same time in the controls with the *Anopheles maculipennis*, the parasites were demonstrated successfully eight times.

In the summer of 1900, ten attempts to successfully inoculate females of *A. punctipennis* were also made by me.* The patients all showed numbers of crescents in the circulating blood, as was verified by two other competent observers. At this time, although I carefully followed the directions of Marchiafava, Grassi, Ross and Thayer,[9] my failure was attributed to faulty technique. There was perhaps some reason for this, because experiments with *A. maculipennis*, carried out at that time, were also unsuccessful in six attempts at inoculation, although a seventh one showed some few doubtful-looking sporozoites. The experiments at that time were never persistently carried out and only a note[1] made of them incidentally.

Including these attempts, it would seem to be at least suggestive that in the fifty-eight exposures of female *A. punctipennis* to infection with estivo-autumnal malaria having crescents in the peripheral circulation, no parasites were ever demonstrable in the intestinal wall, body cavity or salivary tubules. In order to present the results graphically the following rough diagrams have been arranged. The incubation time after the mosquito had satiated itself with the patient's blood, the presence or absence of parasites in the dissected mosquitoes, their anatomical position *in situ*, and the stage of development are given.

* At the Johns Hopkins Hospital.

CASE A. ÆT. 34. M. CRESCENTS IN GREAT NUMBERS.

	Parts Bitten.	Incubated 30° C.	Parasites.	Where Found.	Stage of Development.	
1. *A. Punctipennis*	Thumb	48 hrs.	0	0	0	
1. *A. Maculipennis*	Thumb	48 hrs.	0	0	0	
2. *A. Punctipennis*	Ear lobe	3 days	0	0	0	
2. *A. Maculipennis*	Ear lobe	3 days	0	0	0	
3. *A. Punctipennis*	Ear lobe	4 days	0	0	0	
3. *A. Maculipennis*	Ear lobe	4 days	+	Muscular wall of intestine	Well defined capsulated parasite	
4. *A. Punctipennis*	Ear lobe	4 days	0	0	0	
4. *A. Maculipennis*	Ear lobe	4 days	0	0	0	
5. *A. Punctipennis*	Ear lobe	3 days	0	0	0	
5. *A. Maculipennis*	Ear lobe	3 days	0	0	0	Thirteen tests with each *A. punctipennis* *A. maculipennis*
6. *A. Punctipennis*	Thumb	3 days	0	0	0	
6. *A. Maculipennis*	Thumb	3 days	0	0	0	
7. *A. Punctipennis*	Back of wrist	4 days	0	0	0	
7. *A. Maculipennis*	Back of wrist	4 days	0	0	0	Three successful inoculations of *A. maculipennis*
8. *A. Punctipennis*	Back of hand	5 days	0	0	0	
8. *A. Maculipennis*	Back of hand	5 days	0	0	0	
9. *A. Punctipennis*	Back of hand	5 days	0	0		
9. *A. Maculipennis*	Back of hand	5 days	+	Buds from intest. wall	Reticulated capsulated parasite	
10. *A. Punctipennis*	Back of hand	5 days	0	0		
10. *A. Maculipennis*	Back of hand	5 days	+	Buds in intest. walls	Capsular nucleated masses	
11. *A. Punctipennis*	Back of hand	7 days	0	0	0	
11. *A. Maculipennis*	Back of hand	7 days	0	0	0	
12. *A. Punctipennis*	Back of hand	7 days	0	0		
12. *A. Maculipennis*	Back of hand	7 days	0	0		
13. *A. Punctipennis*	Back of hand	7 days	0	0		
13. *A. Maculipennis*	Back of hand	7 days	0	0		

CASE B. M. ÆT. 29. W. CRESCENTS IN BLOOD.

	Parts Bitten.	Incubated 30° C.	Parasites.	Where Found.	Stage of Development.	
1. *A. Punctipennis*	Back of hand	5 days	0	0	0	
1. *A. Maculipennis*	Back of hand	5 days	0	0	0	
2. *A. Punctipennis*	Back of hand	5 days	0	0	0	
2. *A. Maculipennis*	Back of hand	5 days	0	0	0	
3. *A. Punctipennis*	Back of hand	5 days	0	0	0	
3. *A. Maculipennis*	Back of hand	5 days	0	0	0	
4. *A. Punctipennis*	Lobe of ear	5 days	0	0	0	
4. *A. Maculipennis*	Lobe of ear	5 days	0	0	0	
5. *A. Punctipennis*	Lobe of ear	7 days	0	0	0	
5. *A. Maculipennis*	Lobe of ear	7 days	0	0	0	
6. *A. Punctipennis*	Lobe of ear	9 days	0	0	0	9 experiments with *A. punctipennis*
6. *A. Maculipennis*	Lobe of ear	9 days	0	0	0	
7. *A. Punctipennis*	Lobe of ear	3 days	0	0	0	
7. *A. Maculipennis*	Lobe of ear	3 days	0	0	0	9 experiments with *A. maculipennis*
8. *A. Punctipennis*	Thumb	4 days	0	0	0	
8. *A. Maculipennis*	Thumb	4 days	0	0	0	
9. *A. Punctipennis*	Back of hand	3 days	0	0	0	
9. *A. Punctipennis*	Back of hand	3 days	0	0	0	

CASE C. F. COL. ÆT. 24. CRESCENTS PRESENT.

	Parts Bitten.	Incubated 30° C.	Parasites.	Where Found.	Stage of Development.	
1. *A. Punctipennis*	Lobe of ear	3 days	0	0	0	
1. *A. Maculipennis*	Lobe of ear	3 days	0	0	0	
2. *A. Punctipennis*	Back of hand	3 days	0	0	0	
2. *A. Maculipennis*	Back of hand	3 days	0	0	0	
3. *A. Punctipennis*	Back of hand	4 days	0	0	0	
3. *A. Maculipennis*	Back of hand	4 days	0	0	0	
4. *A. Punctipennis*	Lobe of ear	4 days	0	0	0	
4. *A. Maculipennis*	Lobe of ear	4 days	0	0	0	
5. *A. Punctipennis*	Back of hand	5 days	0	0	0	Twelve attempts with each *A. punctipennis* *A. maculipennis*
5. *A. Maculipennis*	Back of hand	5 days	0	0	0	
6. *A. Punctipennis*	Back of hand	5 days	0	0	0	
6. *A. Maculipennis*	Back of hand	5 days	+	Beeds from intestine	Capsular, nucleated parasites	Two successful infections of *A. maculipennis*
7. *A. Punctipennis*	Back of hand	6 days	0	0	0	
7. *A. Maculipennis*	Back of hand	6 days	0	0	0	
8. *A. Punctipennis*	Back of hand	5 days	0	0	0	
8. *A. Maculipennis*	Back of hand	5 days	0	0	0	
9. *A. Punctipennis*	Back of hand	7 days	0	0	0	
9. *A. Maculipennis*	Back of hand	7 days	0	0	0	
10. *A. Punctipennis*	Back of hand	7 days	0	0	0	
10. *A. Maculipennis*	Back of hand	7 days	0	0	0	
11. *A. Punctipennis*	Back of hand	7 days	0	0	0	
11. *A. Maculipennis*	Back of hand	7 days	+	Intestinal wall	Capsulated parasite with sporozoites	
12. *A. Punctipennis*	Ankle	7 days	0	0	0	
12. *A. Maculipennis*	Ankle	7 days	0	0	0	

CASE D. M. W. ÆT. 60. CRESCENTS IN GREAT NUMBERS.

	Parts Bitten.	Incubated 30° C.	Parasites.	Where Found.	Stage of Development.	
1. *A. Punctipennis*	Palm of hand	4 days	0	0	0	
1. *A. Maculipennis*	Palm of hand	4 days	+	Intestine	Capsulated parasites	
2. *A. Punctipennis*	Back of hand	4 days	0	0	0	
2. *A. Maculipennis*	Back of hand	4 days	0	0	0	
3. *A. Punctipennis*	Lobe of ear	4 days	0	0	0	
3. *A. Maculipennis*	Lobe of ear	4 days	0	0	0	
4. *A. Punctipennis*	Back of hand	4 days	0	0	0	Twelve exposures of *A. punctipennis* *A. maculipennis*
4. *A. Maculipennis*	Back of hand	4 days	0	0	0	
5. *A. Punctipennis*	Back of hand	4 days	0	0	0	
5. *A. Maculipennis*	Back of hand	4 days	0	0	0	
6. *A. Punctipennis*	Back of hand	7 days	0	0	0	Three successful infections in *A. maculipennis*
6. *A. Maculipennis*	Back of hand	7 days	0	0	0	
7. *A. Punctipennis*	Back of hand	7 days	0	0	0	
7. *A. Maculipennis*	Back of hand	7 days	0	0	0	
8. *A. Punctipennis*	Back of hand	8 days	0	0	0	
8. *A. Maculipennis*	Back of hand	8 days	+	Intestine and body cavity	Liberated sporozoites	
9. *A. Punctipennis*	Back of hand	8 days	0	0	0	
9. *A. Maculipennis*	Back of hand	8 days	0	0	0	
10. *A. Punctipennis*	Back of hand	9 days	0	0	0	
10. *A. Maculipennis*	Back of hand	9 days	0	0	0	
11. *A. Punctipennis*	Back of hand	10 days	0	0	0	
11. *A. Maculipennis*	Back of hand	10 days	+	Salivary tubules Body cavity	Numbers of free sporozoites	
12. *A. Punctipennis*	B'k of fo'arm	10 days	0	0	0	
12. *A. Maculipennis*	B'k of fo'arm	10 days	0	0	0	

CASE E. M. W. ÆT. 21. CRESCENTS FOUND ONCE.

	Parts Bitten.	Incubated 30° C.	Parasites.	Where Found.	Stage of Development.	
1. *A. Punctipennis*	Back of hand	48 hrs.				
A. Maculipennis	Back of hand	48 hrs.				
A. Punctipennis	Lobe of ear	48 hrs.				
A. Maculipennis	Lobe of ear	48 hrs.				

The patient did not return to the dispensary

The last patient entered very enthusiastically into the plan, but did not return to the dispensary for many weeks subsequent to his first appearance. The parasites had then disappeared from his blood.

It was found that the bites on the dorsal surface of the hands annoyed the patients least. These itched less, the swelling disappeared more quickly and the bites were more amenable to treatment in this position. It was sometimes found necessary to produce four or five bites at one time. The part was then wrapped in sterile gauze moistened in ammonia or bicarbonate of sodium with glycerine. The itching and œdema usually disappeared very quickly.

The evident difficulty experienced in obtaining successful inoculations of *A. maculipennis* militates somewhat against the conclusion that *A. punctipennis* does not transmit or propagate the plasmodia of estivo-autumnal malaria. Taken, however, with the geographical distribution of malaria and *Anopheles punctipennis,* and the absence of any reference whatever in the literature of this species as having been found with parasites, it would seem to be at least strongly corroborative. Farther than this I do not claim to go.

In concluding I desire to express my appreciation to Dr. William F. Lockwood, Professor of Clinical Medicine of the College of Physicians and Surgeons, and to Dr. Samuel T. Darling, Resident Pathologist of the Baltimore City Hospital, for their kind assistance in this study.

Literature.

1. L. K. Hirshberg and G. C. Dohme: Johns Hopkins Hospital Bulletin, Feb.-March, 1901.

2. Journal of Hygiene, Vols. I and II.

3. L. O. Howard: Mosquitoes. New York, 1901.

4. Journal of Hygiene, Vol. I, No. 1.

5. Grassi, B.: Venti specie di Zanzare Italiene Classate e descritte e indicate secondo la loro distribuzione corologica. Bull. d. Soc. Entomol. Italiana, Vol. XXXI, pp. 46. Florence.

6. W. S. Thayer: As quoted in (1).

7. R. Ross: Deutsch. Med. Woch., Jahr., XXVIII, p. 231.

8. Marchiafava and Bignami: Twentieth Century Practice, Malaria, Vol. XIX.

9. W. S. Thayer: New Orleans Med. Journ., Sept., 1901.

Additional Literature not Cited in this Text.

W. S. Thayer: Lectures on Malarial Fevers, 1897.

S. Coronado: Cronica Medici Sururgica de la Habana, Nov., 1892.

A. Lavaran: Comptes Rendus, Soc. de Biologie, No. 14, June 9, 1900.

Marchiafava, Bignami and Mannaberg: New Syd. Soc., 1894.

W. Osler: Trans. Phila. Path. Soc., Vols. XII and XIII.

G. H. F. Nuttall: Centralbl. f. Bakteriol. u. Parasitenk., XXVII.

W. N. Berkeley: Laboratory Work with Mosquitoes. New York, 1902.

C. W. Stiles: Virginia Semi-monthly, Vol. VI, pp. 53-58.

E. Sergent and Et. Sergent: Observ. sur les Anopheles de la banlieue de Paris. Ann. de l'Inst. Pasteur, Vol. XVI.

J. Levick: Rôle of Mosquitoes in Malaria. Proc. Birmingham Nat. Hist. and Philos. Soc., Vol. XI, Pt. 2, 1901.

B. Galli-Valerio: Gegenwärtigen Stand unsere Kentnisse der Malaria. Therapeutische Monatsschr., 1901.

L. Pagliani: "Lotta centro la malaria secondo le cognizioni odierne, sulla sua causa e modo di trasmissione." Atti della Soc. Piemontesse d'Igiene, Anno XI, 1901.

Von Wasielewski: Hygienische Rundschau, Vol. XI, pp. 675.

H. Ziemann: Beitrag zur Anopheles-Fauna. Archiv f. Schiffs- u. Tropen-Hygiene, Vol. VI, pp. 360-361.

J. C. Thompson and T. M. Young: Journ. Trop. Med., Vol. IV.

F. Martirano: Atti d. Soc. p. g. Studi Malaria, Vol. III, pp. 391.

F. Martirano: Deutsch. Med. Wochenschr. Jahrb., XVIII, p. 786.

F. Martirano: Zeitschr. f. Hyg., Vol. XLI, pp. 147-152.

S. P. James: Malaria and Anopheles in India. Memoirs of Med. and San. Dptmts. of India, No. 2, New Series.

H. F. Cassidy and F. C. Bayne: Differentiation of Anopheles. American Medicine, May 24, 1902.

C. A. Bently: Anopheles in Tezpur, Assam. Ind. Med. Gazette, Vol. XXXVII, pp. 15-16.

A. D. de Grandpré and D. d'E. de Charmey: Les Moustiques. Port Louis, 1900.

C. W. Daniels: Breeding Grounds and Development of Crescents in Anopheles.

Reports to Malaria Committee, 5th Series.

G. H. F. Nuttall and A. E. Shipley: Structure and Biology of Anopheles: Maculipennis. (With Bibliography.) Journ. Hygiene, Vol. II, No. 1, Jan. 1902; Vol. III, No. 2.

G. H. F. Nuttall, Louis Cobbett and T. Strangeway-Piggs: Journ. of Hygiene, Vol. I, Nos. 1 and 2. (Complete literature.)

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

October 12, 1903.

The following officers were elected for the ensuing year: President, Dr. Thomas B. Futcher; Secretary, Dr. Charles P. Emerson.

Demonstration of Medical Cases. DR. MCCRAE.

Twice within the past two years I have exhibited before this Society a man suffering with aneurism of the thoracic aorta, who presented very unusual features. We presented the case as one of "wandering aneurism," for want of a better name.

The patient was a colored man, 49 years of age when admitted the first time in December, 1901. His previous history was negative. Three months before admission he had caught cold, there had been a cough and a great deal of pain in the chest. Examination showed nothing unusual except slight dulness on percussion to the left of the manubrium. He returned to his work, but was readmitted in October, 1902. He then had a pulsating swelling to the right side of the thorax extending from the outer border of the sternum to the nipple line. The pulsation could be seen from the foot of the bed. There was a diastolic shock and a systolic impulse over the tumor. There was no definite pulsation to the left of the sternum. On October 17 we noted that the swelling was rather less, but it was present until the 19th, on which day it was observed at ten o'clock, but had completely disappeared at noon, and there was then a swelling to the left of the sternum; that is, the prominence had moved from one side of the thorax to the other. The blood pressure then became markedly less in the left radial artery. On October 30 the visible tumor again moved from the left to the right side and this condition persisted until his discharge on the 31st of December. At that time the patient was shown here, and there was some discussion regarding it, but no one had any satisfactory explanation to offer.

His third admission was in March, 1903, when there was a marked precordial bulging, systolic retraction and other signs of adherent pericardium. The swelling was now on the left side again, but within a month it moved to the right once more and remained that way until death. For some months the dulness over the left side increased very markedly.

We always hope that the autopsy will clear up anomalous symptoms of this kind, but that we were able to do so in this case is very doubtful. I have the specimen of the aneurism, but cannot tell why it moved about from side to side. The heart, aorta and lungs were removed *en masse* and you can see the relation of all these. The aneurism is directly above the heart and the lungs are pushed aside. It arose from the arch above the aortic valves. The portion to the right, which came well over to the right margin of the sternum, and which corresponded to the area where the pulsating tumor appeared, is very thin. Below and to the right it is filled with clot. There is adherent pericardium and the lungs showed marked adhesions as well.

The only explanation I can offer for the sudden appearance of the tumor to the right is that there had been probably a sudden extension in size of the aneurism, represented by this thin-walled portion, but, of course, this is only conjecture. As to why it should disappear on the right and move to the left side, I cannot say. The apex of the heart moved definitely across when the aneurism shifted to the right, and possibly it was only the varying relationship between the heart and lungs, from the pressure, that gave the impression of moving. One interesting point was the fact that death seemed directly due to rupture into the pericardium behind, where it was not adherent. The trachea shows some signs of erosion, and the probability is that before long there would have been a perforation. The left lung is very much contracted, practically imbedded in adhesions, and the bronchi were filled with purulent material, but there was no cough and no gangrene. There was a second aneurism of the descending portion of the arch. Sections of the lung show extreme collapse and resemble connective tissue instead of cells.

DISCUSSION.

DR. FUTCHER.—One feature of interest in the case was brought out by the X-ray photographs. Two or three different photographs were made and with the shifting in the position of the pulsation there always seemed to be a corresponding change in the position of the shadows as seen on the plates.

The patient had pretty definite symptoms and signs of adherent pericardium and, as you will see from the specimen, the parietal pericardium was almost completely adherent to the visceral.

Demonstration of Surgical Cases. DR. FOLLIS.

The first patient was a woman, aged forty-five, who was brought to the Hospital with a wound in the right lumbar region caused by a 38-caliber revolver. Her last meal had been taken four hours before admission, and she was seen two hours after the accident. Examination showed abdominal rigidity, normal temperature, and leucocytosis of 30,000. The abdomen was opened through the right rectus, and the cavity found full of bloody fluid and bowel contents. Eleven intestinal and six mesenteric perforations were found. Two in the cecum and two in the ileum were closed. The portion of gut containing the seven remaining perforations was excised, and the two bowel ends left in the abdominal wall. The patient reacted well, and her condition was good for two weeks, but on account of her failing nutrition (due to the loss of fluid matter through the high fecal fistula), an extra

peritoneal lateral anastomosis was done by the elastic-ligature method. The patient did well, and after six weeks the bowel ends were excised and turned in under cocaine.

The second case was a colored boy, aged ten years, who was admitted with typical signs of peritonitis and of typhoid fever, including a positive Widal. He was immediately explored, and an intestinal perforation found about 25 cm. above the ileo-cecal valve. The ends of the bowel were brought to the abdominal wall and left there. The patient had a post-operative pneumonia of the right side, developed a large abscess of the right thigh, subsequently suffered acute intestinal obstruction due to the omentum, and was sick with the measles for one month. The enterostomy wound was fully closed under cocaine, and the patient recovered completely. Enterostomy in general peritonitis, with distention, is not a new procedure, having been done by Doyen of Paris, and from one of the Vienna clinics we are told that a typhoid perforation should never be closed, but should be left as a natural avenue for drainage.

Discussion.

Dr. McCrae.—Dr. Follis is to be congratulated on his good result, and there is one lesson to be learned from this boy—that the typhoid patient with perforation should be given the chance of benefit by operation even when general peritonitis is well advanced. We had thought there was almost no chance of saving this boy. During the last year we have had three cases admitted with general peritonitis and all were operated upon, with the result of saving one out of the three. Curiously enough, our surgical record on all cases of typhoid perforation is a saving of just that proportion—33⅓ per cent.

October 26, 1903.

The meeting was called to order by the President, Dr. T. B. Futcher.

Some Recent Cases of Extra-uterine Pregnancy. Dr. Cullen.

I shall mention only the salient details in each case.

Case I.—Mrs. H., about 30 years of age, admitted to the Johns Hopkins Hospital July 18, 1903. This patient had been nursing a young child and has not been menstruating. For several weeks there has been very severe pain in the left iliac region. On making a vaginal examination under ether the pelvis was found to be partly filled with an irregular mass which broke up readily under the finger, strongly suggesting pelvic clots occurring where rupture of a tubal pregnancy had taken place.

July 20.—On opening the abdomen I found a ruptured extra-uterine pregnancy on the right side. The tube near its outer end was fully 2.5 cm. in diameter. The pelvis was filled with tarry-looking clots and there was also some free blood in the abdomen. The tube was removed, the clots washed out with salt solution and considerable solution was left in the abdominal cavity. Recovery normal.

In this case, as the patient was nursing her child and not menstruating, we had not this sign to determine whether pregnancy existed. The rupture had evidently been a small one and the loss of blood gradual, as the patient gave no distinct signs of internal hæmorrhage.

Case II.—Mrs. H., aged 35, seen in consultation with Dr. Robert Hoffman July 20, 1903. There was a cessation of the flow for at least two and a half months and then a bloody discharge for a few days. While standing at a table she had a sudden and severe pain, especially in the left lower abdomen, and was compelled to drop to the floor. She was exceedingly pale and the abdomen swelled up "like a barrel." The abdominal distention gradually subsided, the pallor lessened and she was able to move around. The uterus was slightly enlarged and to the left was a definite mass fully as large as a baseball. I advised immediate operation. On opening the abdomen the left tube was found above the pelvic brim and adherent to the mesentery of the small intestine. In the abdomen there was considerable blood fluid. The left tube near its proximal end was normal in caliber, but in the vicinity of the fimbriated extremity 2.5 cm. in diameter and ruptured over an area 3 cm. Here the placental tissue was projecting through and the fœtus had escaped. The pelvis was filled with clots. The tube was removed and the pelvis irrigated with salt solution. On the left side of the bladder was a roughened area 4 x 5 cm. where the blood clot had partially organized. It was impossible to peel this off without leaving a bleeding surface. It was therefore not disturbed. The abdomen was closed without drainage. Recovery normal.

This case demonstrates what large hæmorrhages may occur and yet the patient finally recover. I have noticed that where the patient is a nullipara and has firm abdominal walls that the hæmorrhage is not as a rule very severe, as in a short time the abdominal cavity is full and no more bleeding can take place. In those women where the abdominal walls are very lax the abdomen can accommodate a great quantity of fluid and fatal hæmorrhages are more prone to occur.

Case III.—Mrs. S., aged 30, seen July 29, 1903, with Dr. James Linthicum. The patient was perfectly well until three weeks ago, when, while running a sewing machine, she suddenly experienced severe pain in the right iliac fossa. She soon became blanched and was forced to go to bed. Once or twice since then there have been paroxysms of pain accompanied by weakness. Since the first appearance of pain there has been a bloody vaginal discharge and a great deal of discomfort in the right iliac region. The cervix is rather soft, the uterus slightly enlarged. To its right is an irregular mass the size of a small cocoanut. Extra-uterine pregnancy was diagnosed and operation advised.

We found some free blood in the abdomen and on drawing the omentum back discovered a pregnancy in the right tube. At the uterus the tube was normal in size but rapidly dilated, forming a mass 5 cm. in diameter. Anteriorly this was intact, posteriorly blended with the omentum, small intestine and large blood clot. The right tube and a portion of the ovary were removed. Recovery normal.

In this case there was not the slightest suspicion of pregnancy until rupture of the tube occurred.

Case IV.—Mrs. S., aged 28; admitted to the hospital August 3, 1903. Since her last period, one month ago, there has been a continual hæmorrhagic vaginal discharge. For three weeks she has complained of constant pain in the left ovarian region and since the flow came on this pain has become excessive. She came saying that for the last 24 hours the pains had been "labor-like" in character and she felt that "something must come away." On examination I found the uterus very little enlarged, but on the left side an indefinite thickening could be detected. More accurate details could not be obtained on account of the thick abdominal walls.

Three hours later on opening the abdomen I found the left tube much altered. Near the uterus it was 5 mm. in diameter but rapidly increased in size and at its fimbriated extremity it was adherent and reached 2.5 cm. in diameter. It was dark blue in color and filled with blood. It was a very early tubal pregnancy. Both tubes were removed, as the right was occluded, due to an old inflammatory process.

The recovery was a normal one. In this case the history was so characteristic that a fairly accurate diagnosis was possible before rupture.

Case V.—Mrs. W., about 35 years of age, seen with Dr. Thomas Talbott, August 16, 1903. For the last month this patient has had a faint hæmorrhagic discharge. Less than 48 hours ago she was seized with pain in the right ovarian region. The pain was paroxysmal in character and so severe that morphia did not control it. She herself said that the pains were "labor-like" in character. There was no elevation of temperature. At 10 P. M. her pulse was 80. When I saw her two hours later the pulse was 100 and some pallor was evident. On vaginal examination there was a faint evidence of thickening on the right side and I confirmed the diagnosis which Dr. Talbott had already given. We were also of the opinion that rupture had taken place after 10 P. M. on account of the quickened pulse, the pallor and the coincident cessation of pain. She was immediately removed to the hospital, and as the pulse was of good volume and did not become more rapid, operation was deferred until morning. On opening the abdomen the tell-tale dark bloody appearance was evident. The right tube at its uterine end was normal about 1.5 cm. distal to the cornu, became fully 2 cm. in thickness and had a markedly bluish appearance. At one point on the posterior surface was a small rupture; the fimbriated end of the tube was normal. The tube contained an intact placenta and a very small fœtus (Fig. 1). The abdominal cavity contained fully 500 cc. of clots and in the region of the liver and also on the left side was considerable blood. The abdominal cavity was irrigated and closure was followed by normal recovery.

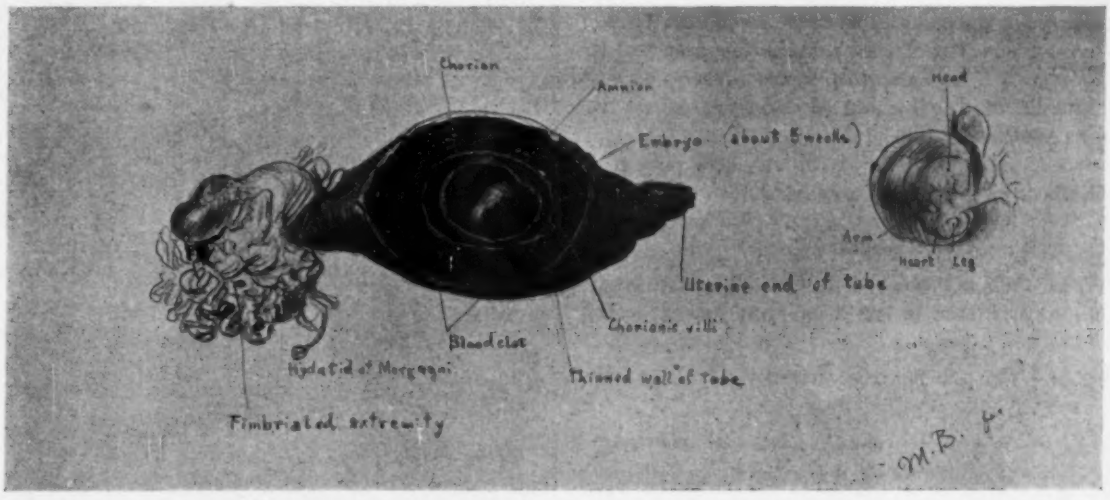

FIG. 1.—Tubal pregnancy with placenta, membranes and foetus intact (natural size). The uterine and fimbriated ends of the tube are normal. Occupying the centre of the tube is an early pregnancy. The placenta and membranes are clearly outlined. The foetus is nearly 1 cm. in length.

This is also another example of an extra-uterine pregnancy presenting a typical history, and Dr. Talbott deserves much credit for having made the diagnosis prior to rupture. It is exceptional to find such a perfect fœtus in a tubal pregnancy.

Case VI.—Mrs. H., aged 34, seen with Dr. Ernest Johnston, of Berkeley Springs, W. Va., September 30, 1903. The patient has had six children; the youngest is 11 months old. She has had no periods since the birth of the last child. Four weeks ago she was seized with severe cramp-like pains coming on suddenly while standing in a store. Ever since then there has been a bloody vaginal discharge. When the cramps first came on she became very pale. On examination under ether I found the cervix hard, the uterus slightly enlarged and a nodule above and to the right of the right cornu; it felt very much like a myoma. Douglas' pouch was filled

with an ill-defined mass. I could not tell whether we were dealing with a myomatous uterus associated with pelvic peritonitis or with an extra-uterine pregnancy. Dr. Johnston, however, felt sure that it was a tubal pregnancy. On opening the abdomen we immediately encountered dark blood. What was supposed to be a myomatous nodule was an enlarged right tube, which was fully 5 cm. in diameter and somewhat kinked. The pelvis was filled with tarry blood. The tube was removed. Recovery normal.

This case is also interesting on account of the fact that the patient was still nursing her babe and was not menstruating, and consequently there was no menstrual clue.

While it is exceptional to see so many cases of tubal pregnancy in so short a period, yet I think we must admit that this disease is a common one and that in all probability many cases have been overlooked. Undoubtedly there are cases where no symptoms are manifest until rupture of the tube has occurred, yet in the majority of cases the clinical picture is characteristic, and I feel sure that in the near future many more cases will be recognized before rupture has occurred. Even in this small group of cases, two out of six were detected before hæmorrhage developed.

In all of our cases placental tissue was detected either macroscopically or on histological examination.

Discussion.

Dr. Osler.—I do not think that these cases were overlooked previously; I used to see them—post mortem—that was a very common experience.

Dr. Cullen.—But post mortems were not very frequently made until recently.

Dr. Osler.—Yes, but even among those that were made they were common, and those of you who can go back, say 25 years, will remember that ante-mortem diagnosis was very rare. At the Day of Judgment, when gynæcologists have to confess their sins of omission and of commission, we shall see the figure of Lawson Tait rise up in vindication, and their sins will be blotted out for the sakes of the lives of women they have saved in the class of cases described by Dr. Cullen this evening.

Dr. Cullen.—Dr. Osler having alluded to Lawson Tait in this connection, I want to add that we owe more to him than to any one else for the development of knowledge on this subject.

A Case of Typhoid Arteritis. Dr. Walter R. Steiner.

The patient was a boy, aged nine years, who had a very severe infection of typhoid fever, followed by two relapses. In the interval between the two relapses, on the forty-first day of the disease, an arteritis of the right axillary, brachial and radial arteries was noted. The pulse was wanting in the axillary vessel for three days, but in the brachial and axillary arteries thirty-five days had elapsed before it was again felt. The return of pulsation was complete in all of these arteries.

Discussion.

Dr. Thayer.—In connection with this remarkable case it will be remembered that we have had several similar instances in the hospital—cases which I brought together last year.

In considering the question of the vascular complications of typhoid fever within the last year I have been impressed with their frequency and importance. Typhoid fever not only plays an important part in the production of phlebitis and arteritis in smaller vessels, but it is not improbable that it sometimes gives rise to more extensive and widespread changes in the arterial system. Some clinical studies upon our old typhoid fever patients which I have recently been making, and which I hope soon to report, indicate that typhoid fever plays a definite rôle in the etiology of arteriosclerosis.

Potain has described acute aortitis occurring in the course of typhoid fever which he believes is susceptible to recognition during life. I have never seen such a case.

Dr. Osler.—How did you account for the favorable change? Was it by anastomosis?

Dr. Steiner.—I thought it was simply that the inflammation subsided in the arteries.

Dr. Osler.—That is probably the best explanation; that the occlusion was simply due to swelling of the walls—without thrombosis. It is difficult to suppose that it was by anastomosis, and I do not think that canalization ever takes place to the extent of restoration of a full pulse.

Some observations have been made lately as to the action of lime salts in adding to the coagulability of the blood and assisting thrombosis and suggesting that materials containing an excess of lime should be removed from the diet of these patients.

Dr. Futcher.—Thrombosis of the arteries in typhoid cannot be of such great infrequency as we might at first suppose. Dr. Keen a few years ago collected 115 cases from the literature. In 46 of these the arteries of the lower extremities were involved. In 8 the thrombosis was bilateral; in 19 right-sided and in 19 left-sided. This is in contrast to what one finds in venous thrombosis of the lower extremities, where the left side is much more frequently affected than the right.

Dr. Thayer.—How great the real and apparent occlusion of an artery may be from simple swelling of the walls is shown by an observation of Tuthill (Trans. Med. Soc. N. Y., Syracuse, 1885, 222), who states that in a leg amputated for gangrene the only artery found pervious was the posterior tibial, from which the blood escaped in "fine needle-like jets." In such an artery it is highly probable that the pulsation would be entirely impalpable.

In connection with this it may be of interest to mention a very remarkable case, the report of which was given to me recently by Dr. Royster, of Norfolk. The case was that of a little girl of eight, who, two years ago, toward the end of a rather severe typhoid fever, became suddenly unconscious and presented rigidity of the neck, paralysis of the left side, the face, arm and leg, together with paralysis of the third nerve on the right side. After several days, the paralysis

cleared up, but since then, at various intervals, there have been typical attacks of Jacksonian epilepsy with spasm of the left side of the body and of the right lid and pupil.

DR. PLEASANTS.—I would like to ask Dr. Steiner if it is not possible that he had to deal here with thrombosis of the vein, which by pressure on the artery would have produced this condition?

DR. STEINER.—I do not think that thrombosis of the adjacent vein would have obliterated the pulse entirely. Dr. Janeway thought there was no doubt about the presence of arteritis, and while the pulse recurred in the axillary artery in three days it did not return in the radial and brachial until the lapse of 35 days.

The Treatment of General Infections, with Especial Reference to the Use of Silver Nitrate in Such Cases. DR. JOSEPH HUME.

DISCUSSION.

The surgical treatment of general infection aims at free drainage, stimulation and increased elimination. The injection of salt solution, the administration of antitoxines, and the introduction of antiseptics into the blood illustrate these fundamental principles. It has often been observed that infection causes a rise in the leucocyte count. It therefore seemed that possibly an effort artificially to increase the white blood count was indicated. Silver nitrate has this effect, and hence it has been used in the treatment of infections. Possibly it does good by destroying the blood corpuscles and setting free anti-bodies. If so, a new principle in therapeutics has been established, namely, the introduction into the blood of a hemolytic agent. In the series of cases here reported 1 cc. of a 10 per cent solution of silver nitrate was mixed with 1000 cc. of water. Of this mixture 500 cc. was injected intravenously at a temperature of 110° to 115.° A chill, rise in temperature, marked drop in the leucocytes, followed by profuse sweating, were the phenomena observed in all cases. Several characteristic cases were reported. The first was a girl, aged sixteen years, suffering from streptococcus infection following an appendectomy. The usual surgical treatment did no good; the patient became extremely toxic, but following two injections of silver nitrate recovered completely. The second was a patient with a large peritoneal abscess, probably a general peritonitis. She was weak and irrational, and became rapidly worse in spite of treatment. The temperature had reached 104.° Silver nitrate was given three times, with the usual phenomena following. After each injection there was some improvement, and the patient was finally discharged well. Another case of streptococcus infection, very toxic and delirious, was similarly treated, and after the third injection made a perfect recovery. Ten cases of pyogenic infection have been treated by Dr. Hume with silver nitrate. He has had but one death, and that from intercurrent infection. No local results have been observed except two cases of mild phlebitis.

DR. OSLER.—I would like to ask, in view of these extremely good practical results, whether the treatment is of any value in cases of endocarditis, for silver has been recommended as giving good results in this disease, I believe.

I would also like to ask if it is not superfluous to open the vein for making these injections; is it not sufficient to insert the needle directly into the vein without an incision?

DR. HUME.—In most of the cases in which we have employed this method, the circulation has been so bad that even after lowering the arm over the side of the bed, the veins do not dilate enough to enable you to introduce the intravenous needle without making an incision and exposing the vein.

DR. THAYER.—Dr. Hume's observations are of great interest, more especially from a practical point of view. Why this procedure should be followed by favorable results, however, I cannot see. Theoretically, I cannot see why the destruction of red blood corpuscles or leucocytes should necessarily increase the resisting power of the organism. Certainly there can be no question of the production by such a method of specific anti-bodies.

Dr. Hume's results are interesting not only in themselves, but in the effect which they have produced upon those who have observed the cases. It seems to me, however, that further observations as well as animal experiment will be necessary before one can express a positive opinion as to the value of this procedure.

DR. GORTER.—In one of my cases of typhoid, Dr. Hume gave nitrate of silver as a last resort. It was apparently only a question of a few minutes before the patient must die, but revival occurred in the most wonderful way after the injection.

DR. COLE.—It is quite certain that the decision as to the value of this method of treatment must depend more on clinical observations than on any theoretical considerations. But in drawing conclusions from clinical observation, great caution must be observed. This is especially true in regard to streptococcus infections, for it is now known that many of these cases recover, even after a general invasion of the body, as shown by blood cultures, has occurred.

Bertelsmann (Arch. f. klin. Chir., Bd. 67) has published the results of bacteriological blood examinations in a series of surgical cases. Among his cases were 27 in which streptococci were demonstrated in the circulating blood during life, and of these cases, 19 recovered.

Among the cases of general streptococcus infections with recovery, occurring in this hospital, one treated during the past summer is of especial interest. This was in a young man admitted to the surgical service with a history of having been struck on the head by falling bricks five days before admission. Notwithstanding the fact that the scalp injury seemed trifling, the patient's condition had gradually grown worse. He complained of pain in his head, his temperature became elevated and he was therefore brought to the hospital. On admission his temparature was 106°, and, thinking that this might be due to an infection in the scalp wound, this was freely opened and swabbed with pure carbolic acid. His condition, however, did not improve. The temperature

ranged between 102° and 105°, though the pulse rate remained about normal. He was then transferred to the medical side with a probable diagnosis of typhoid fever. The Widal test, however, was negative, and blood cultures showed the presence of *Streptococcus pyogenes*. The fever continued high for over two weeks. He was desperately ill, so that his life was despaired of, and we were about proceeding to some more active measures, such as that discussed by Dr. Hume, when, without any special treatment, the temperature began to fall, his condition improved and complete recovery followed. Blood cultures on three occasions showed the growth of a pure culture of *Streptococcus pyogenes*, so that there can be no doubt as to the diagnosis. There was no cardiac involvement and the Widal test remained persistently negative. This case well shows the danger of drawing conclusions from a few cases as to the efficacy of therapeutic procedures.

As to the theoretical considerations, while it has been demonstrated that so-called endo-complements play a part in the action of certain hæmolytic toxins, I know of no experimental basis, and none has been adduced, in support of the supposition that either bactericidal complements or immune bodies may be set free by the disintegration of red blood corpuscles. Moreover, it has been shown by Wassermann and Takaki (Berliner klin. Wochenschrift, 1898) that the immune bodies in typhoid fever take their origin in the lymphatic tissues of the body, so that in this disease, at least, the action of the silver solution, suggested by Dr. Hume and Dr. Pancoast, cannot play an important rôle.

Dr. Emerson.—The clinical side of the subject I am not qualified to discuss, but I would like to say a few words about the chemical action on the blood of the salt solutions, and especially since the previous speakers have brought the theoretical side of the question so much in the foreground. In the first place, there is really no danger that the salt solutions in common use are, because of their low percentage (0.6 per cent NaCl), dangerous. They are dangerous enough without this. While it is true that a solution of 0.9 per cent would more closely resemble the plasma, yet the plasma is hypertonic and the corpuscles are not laked in a watch-glass unless a solution below 0.4 per cent NaCl be used, and it is very doubtful if the blood can be laked within the vessels by the introduction of distilled water.

Again, the previous speakers seem to assume that the introduction of a dilute silver nitrate solution is about the same as if pure water had been used. But this is by no means the case; silver chloride is precipitated, but sodium nitrate is left in solution, and sodium nitrate is not a salt which will aid our friends' theory by causing hæmolysis, nor is it an indifferent salt; in fact, it may be even more beneficial than the sodium chloride which it replaces; at least Dr. Styles, in the Physiological Laboratory of this University, found a Ringer's solution made up with sodium nitrate superior in some ways to that with sodium chloride.

We much doubt, therefore, that hæmolysis has any part in explaining the beneficial results of the silver nitrate infusions. But if you could cause hæmolysis, it would be an event not without considerable danger. In fact, there is but one animal which would suffer worse than man from the potassium salts thus liberated, and that is the rabbit; in the dog the danger from this source is hardly one-twentieth as great; and potassium salts, Dr. Howell has found, have a very deleterious effect on the heart's action.

Lastly, judging from their leucocyte counts, we are told there occurs a destruction, then in a few hours a regeneration, of the white cells. But this is doubtful. This phenomenon—the drop and subsequent rise of leucocytes—has been observed long ago following the injection of various substances, and has been explained quite satisfactorily, first by Goldscheider and Jakob, as a redistribution of these cells; first they accumulate in the internal organs, then the depots of leucocytes in the bone-marrow empty out their cells and the count in the peripheral vessels rises. The formation of new leucocytes follows, but not soon enough to explain the leucocytosis our friends have observed.

Dr. Reik.—I have had the opportunity to observe the effect of this treatment in one case and must say that from the clinical standpoint it seemed marvelous. The case was one of thrombosis of the lateral sinus with general infection resulting from a chronic suppurative otitis media. A mastoid operation was performed and the septic clot removed from the sinus after ligation of the internal jugular. Metastatic abscesses appeared at various places and the patient's condition was so low that Drs. Finney and Pancoast, who saw the case in consultation with me, believed that death was imminent. At Dr. Finney's suggestion Dr. Hume was sent for, and he very kindly administered an intravenous injection of silver nitrate. This was performed about midnight, and when I saw the patient again on the following morning the transformation that had taken place was really startling. The temperature had dropped to normal, the patient was comfortable and cheerful and there was altogether the most remarkable change I have ever observed in any patient under any condition and within such a short time. The progress of this case was very satisfactory for some weeks, but the patient died later of an intercurrent affection.

Dr. Hume.—I would like to say that in presenting this theory I do not pretend to much knowledge concerning the action of silver nitrate in the blood, but only offer a possible explanation of the changes which take place. Practically I know that it gives results.

November 2, 1903.

The meeting was called to order by the President, Dr. Futcher.

Exhibition of Cases of Typhoid Meningitis. Dr. Cole.

Dr. Osler has asked me to speak to-night of a very interesting case of typhoid fever showing symptoms of meningitis, in which the diagnosis of typhoid meningitis was made

by means of lumbar puncture during life. In connection with this case I wish to refer briefly to two other cases exhibiting somewhat similar features.

While nervous symptoms in typhoid fever are common, as the old term, "nervous fever," implies, meningeal symptoms are much less common, and of extreme variety are the cases of true meningitis during typhoid, especially those due to the typhoid bacillus.

The first case was a man aged 35, admitted to this hospital two years ago. The onset of the fever had been three weeks before admission and the course of the disease was uneventful up to the time of his entrance. On admission the patient was dull and drowsy, but not delirious, and there were no signs or symptoms of any meningeal involvement. The Widal test was negative, but the diagnosis of typhoid fever was made positive by the finding of typhoid bacilli in the blood by the method previously described (JOHNS HOPKINS HOSPITAL BULLETIN, Vol. XII, No. 124, p. 203). The day after admission the patient became delirious; a few days later he began having persistent nausea and vomiting. On the tenth day following his admission definite meningeal symptoms were noted. There was some retraction of the head and stiffness of the neck, the knee jerks were slightly exaggerated and there was a definite Kernig's sign. A lumbar puncture was performed and 30 cc. of clear fluid were obtained, in which no bacteria could be demonstrated on cover-slips and only a few polymorphonuclear leucocytes, but in the cultures made from this fluid there occurred a moderately profuse growth of typhoid bacilli. There was an improvement in the patient's mental and nervous condition following the lumbar puncture, but a few days later a profuse crop of boils appeared over the back, and these appeared in successive crops over the entire body, the patient gradually becoming weaker and weaker, until death occurred over a month later. This case is interesting and unusual, not only on account of the meningeal features, but from the fact that the typhoid fever terminated in a staphylococcus septicæmia, as was shown by the growth of Staphylococcus pyogenes aureus in cultures made from the blood on two occasions. Although there is a widely prevalent view, based mainly on the results of cultures made post mortem, that secondary infections during typhoid are common, out of about 150 cases of typhoid fever in this hospital in which cultures have been made from the blood during life, this is the only one in which such a secondary infection has been demonstrated.

The second case was a boy, aged 5 years. He entered the hospital after a six weeks illness associated with continuous fever and accompanied by a swelling and redness of the calf of the left leg. He was very sick on admission, was dull and apathetic, and was passing his urine and feces involuntarily. The phlegmon on his leg was opened and found to be quite superficial. On account of his general condition and the involvement of the leg a septicæmia or pyæmia was suspected, but the Widal test proved to be very positive. On the third day after admission there was noted some retraction of the head and stiffness of the neck and of the extremities. Lumbar puncture was performed and 20 cc. of clear, limpid fluid withdrawn. Only a few leucocytes could be demonstrated in the sediment. In the cultures made from this fluid, however, growth of Bacillus typhosus occurred. Following the lumbar puncture there was some improvement in the mental and nervous symptoms, but the other symptoms continued to grow worse and the patient died one week after admission. An autopsy was performed and characteristic lesions of typhoid fever were found. Permission could not be obtained for an examination of the brain, but a piece of the dorsal cord was removed. This failed to show any demonstrable pathologic changes.

The last case we have had under observation during the past few weeks. The patient was a colored boy, aged 15 years. The onset was with a chill, two weeks before admission. Following this he had a continuous fever and some cough, and two days before admission he became delirious and remained so up to the time of his admission. He was then in a muttering delirium and was very restless, occasionally trying to get out of bed. There was also some retraction of the head. It was thought probable that the condition present was one of general tuberculosis, with tuberculous meningitis. Accordingly a lumbar puncture was performed and 30 cc. of quite clear, colorless fluid obtained. No tubercle bacilli could be demonstrated in the sediment, but, staining with methylene blue, a few short bacilli were seen. Unfortunately, no cultures were made. A few days later the cultivation of typhoid bacilli from the blood gave the first conclusive evidence that the condition present was one of typhoid fever and not tuberculosis. The nervous symptoms became more marked, persistent vomiting occurred, and the retraction of the head and spasm of the extremities became extreme. A second lumbar puncture was performed, and this time the fluid was slightly turbid, and on holding it up to the light a distinct shimmer was seen. Under the microscope it was found that the turbidity was almost entirely due to large numbers of motile bacilli, resembling typhoid bacilli, which cultures later proved them to be. A few days later the patient began having some abdominal symptoms and the possibility of a peritonitis and the advisability of operation were considered, but on account of the patient's condition this did not seem advisable. He died on the following day. At autopsy the characteristic lesions of typhoid fever were found, and also broncho-pneumonia, acute cholecystitis and acute purulent cerebro-spinal meningitis.

NOTE.—The histological study of the brain and cord has not yet been completed, and this, together with a more detailed account of these cases, will be published later by Dr. McCallum and Dr. Cole.

All of these cases showed quite marked meningeal symptoms, and in all the typhoid bacilli were cultivated from the spinal fluid during life, but it must be remembered that only

in the last one is there definite evidence of the presence of a true meningitis. Whether in the first two cases a mild meningitis was present, which in the first case disappeared (as did the symptoms, the patient living for almost a month afterward), or whether the invasion of the spinal fluid by these bacilli and their growing and producing their toxines in this medium may so affect the adjacent nerve cells as to cause the symptoms, is not certain. Cases of very mild early meningitis have been reported by Ohlmacher and Hofmann. On the other hand, the fact that typhoid bacilli have been found in the spinal fluid of these three cases of typhoid fever with marked nervous symptoms within a comparatively short time since we have made a routine of spinal puncture in these cases, makes it appear possible that mere invasion of the spinal fluid by these bacilli may be the cause of the marked nervous symptoms so frequently observed.

That a true suppurative meningitis may be caused by the typhoid bacillus, however, is conclusively demonstrated by the last case.

Discussion.

Dr. MacCallum.—In the case of which Dr. Cole has spoken, there was found at autopsy a fibrino-purulent exudate extending not only over the spinal cord but over the brain, being as usual especially abundant in the sulci. Microscopically, as in the case described by Ohlmacher, the most characteristic lesions are to be found on the vessel walls, where the endothelium is frequently lifted up by accumulations of cells which are sometimes so abundant as to completely obliterate the lumen of the vessel. These cells are apparently chiefly polymorphonuclear leucocytes.

There was in this case also an acute diphtheritic cholecystitis, with deep ulceration of the greatly stretched wall of the gall bladder. Although perforation had not actually occurred, there had apparently been an extension of the inflammation through the wall, for the surface of the gall bladder was covered with a fibrinous exudate. Although the bacilli which alone were present on the thin gummous contents had the appearance of typhoid bacilli, the cultures showed only colonies of colon bacilli.

Dr. Futcher.—I think there is one lesson we have to learn in regard to these cases of typhoid fever with cerebral manifestations, and that is that whenever a patient with a continuous fever and marked cerebral manifestations, comes before one at this season of the year, the possibility of typhoid must be kept in mind. It is a case of this kind, particularly in the country where that possibility is not sufficiently recognized by physicians, that causes a great risk of infection to the surrounding country, by failure to disinfect the dejecta. The early symptoms of typhoid may very closely simulate those of a meningitis and the cerebral type of typhoid must be kept in mind.

The Late Effects of Typhoid Fever on the Heart and Blood Vessels. Dr. Thayer.

(To appear in full in the Johns Hopkins Hospital Reports.)

Discussion.

Dr. Emerson.—For some time I have been interested in the study of albuminuria and I have recently abstracted over 1000 of our hospital cases to get some idea of its occurrence. Since I noted the history of typhoid fever and the presence or absence of arteriosclerosis, it may be interesting to see what relation there is between these figures and those of Dr. Thayer. The first point to be observed was that I must exclude all cases of women, because in getting the age curve it differed so from that of the men that I could not arrange a satisfactory curve for arteriosclerosis. This left me 700 cases, and I count as negative all cases in which there was not a definite history of typhoid or a definite note in regard to the state of the arteries. The age periods used were from 1 to 15 years, 15 to 25, and from 25, in decades, upwards; this division was made because 15 is about the age of puberty and 25 represents the age at which the average man is of settled habits. In the first class, ages from 1 to 15, 9 per cent of the cases showed arteriosclerosis (I am now speaking without reference to typhoid); in the second class, 53 per cent; and in the third class, 62 per cent; from 36-45 years, 71 per cent; from 46-55, 75 per cent; from 56-65, 84 per cent; while at the age of 65 it has reached 100 per cent of palpable arteries. Now a study of the cases with a typhoid history shows, in the first period, none; in the second period, 80 per cent, a gain of 30 per cent; and in the third period, a gain of 10 per cent; at the age of 65 there is again 100 per cent of palpable arteries. In other words, the percentage of those with arteriosclerosis, in persons giving the history of typhoid fever, is in the different age periods from 10 to 50 per cent higher than among all persons having arteriosclerosis counted together, including the typhoids.

There is one point I would like to speak of that interested me immensely, and that is the fact that although typhoid seems to have such a deleterious effect upon the arteries, it does not have any such effect upon the kidneys. We should have expected that it would, because renal changes follow so closely upon the heels of arterial changes. Instead, however, there was, on the other hand, even a lower percentage of kidney trouble among those who had typhoid and arteriosclerosis than among those who had sclerosis without typhoid.

I hope that Dr. Thayer will also speak of the connection with aneurisms. If there can be one case with good evidence of a connection between typhoid fever and the production of aneurism it would be most fortunate for many patients. As it is now, when a young man comes in with an aneurism and denies a history of syphilis, no matter how positively he denies it, we suspect the truth of his statement. We should like to give him the benefit of the doubt.

Dr. Futcher.—Our attention was called at the last meeting to the acute vascular complications that occur in connection with typhoid fever, in Dr. Steiner's paper, and Dr. Thayer at that time recalled the fact that we have had in our typhoid series, three cases of arterial thrombosis. I think the society is much indebted to Dr. Thayer for this careful

piece of work, emphasizing as it does the fact that typhoid during the course of the illness apparently sets up changes in the arteries, that may result in very definite arterial thickening later on in life.

A Preliminary Report on a New Method of Treating Tinnitus Aurium. DR. REIK.

I wish to make but a brief preliminary report at the present time, on some recent experiences in the treatment of that most troublesome symptom in ear diseases—tinnitus aurium—and to suggest a new therapeutic measure for its relief. You are probably all aware of the fact that the list of drugs recommended for the abolition of these distressing subjective sounds is already an unusually long one and not to be thoughtlessly increased, but the very fact that so many things have been proposed, and remain in use, indicates the unsatisfactory nature of the results obtained from their employment. The remedy that I shall ask you to consider in this connection is supra-renal extract and I was first led to use it, about six months ago, as a logical sequence of some experimental work that I had been conducting in the Physiological Department of this University. Before speaking of its practical application, it would be well, perhaps, to say something about the nature and mode of production of these subjective noises.

Tinnitus is defined as a ringing or singing sound in the ears. As a matter of fact, these subjective sounds vary greatly so that scarcely any two persons describe them in exactly the same way. They may be constant or intermittent and are always more or less annoying, sometimes extremely distressing, to the individual affected. They occur in about two-thirds of all cases of ear disease; being present in nearly all cases of acute or chronic catarrhal affections of the middle ear, many of the acute inflammatory conditions of the tympanum, some few of the chronic suppurative processes and, even in a number of cases of irritation of the external auditory canal as, for instance, where there is a mass of cerumen or other foreign body present.

Now the generally accepted explanation of their mode of production has been that the foreign body present in the canal or the inflammatory exudate in the tympanum produced a direct pressure on the tympanic membrane and ossicles, and thus indirectly through the foot-plate of the stapes upon the endolymph of the internal ear, and caused a simulation of the effect of a regular succession of sonorous waves upon the membrane. As you will readily see, this explanation is not an entirely satisfactory one. It may apply to a fair number of cases but there are unquestionably many cases of tinnitus where it would be impossible to prove and unreasonable to presume that any degree of increased intralabyrinthine pressure exists. Besides, in those cases where it may be assumed to have been present the tinnitus often persists long after every evidence of undue pressure upon the ossicles has been removed.

As the result of some experimental work which I have been permitted to conduct in the Physiological Laboratory, I am convinced that the proper explanation of the mode of production of tinnitus lies in an entirely different direction. I shall not attempt to review all of that work to-night but will simply say that animal experimentation has shown very conclusively that any irritation of the tympanic membrane or of the walls or contents of the tympanum will cause a marked vaso-motor disturbance and that this vascular change is invariably in the direction of vaso-dilation; that irritation of the sensory nerves of the tympanum produces a depressor, and not, as might have been expected, a pressor, effect. In the second place, these experiments have shown that any exudate into the tympanum, and here I tried to imitate the pathological conditions that exist in catarrhal affections of the ear, however small, will produce a like effect, and, that this vasomotor change commences with the entrance of the first particle of fluid introduced into the tympanum and before there can be any question of increased intra-tympanic or intra-labyrinthine pressure. It appears that irritation of the tympanum causes a dilatation of the small blood vessels of the middle and internal portions of the ear, and that the sounds produced by the increased flow of blood in the neighborhood of the delicate terminal filaments of the auditory nerve are sufficiently loud to be appreciated by the person so affected, and that sometimes they are sufficiently loud to be heard by the examiner.

Very naturally, if this be the proper explanation of the etiology of tinnitus aurium, the treatment should consist in the employment of some remedy that would tend to raise the blood pressure. Up to the present time I have experimented only with the extract of supra-renal gland, since that is to-day the most highly lauded blood-pressure-raising element. I first tried local applications but without effect. Then I began to administer the tablets or powdered extract, giving from one to two grains three times a day, and this met with more success. Together with the aid of my assistants in the Baltimore Eye, Ear and Throat Charity Hospital and in the Johns Hopkins Hospital Dispensary, I have now employed this treatment in a considerable series of cases but since these cases were all treated in the summer and fall months of a dry season, and the time elapsing since they came under observation has been so short, I am not yet willing to draw any conclusions as to the possible cures or the lasting effects of the remedy. I merely wish to call attention to the new theory, which I shall publish later in more detail, explaining the production of tinnitus, and to the logical conclusion drawn therefrom that tinnitus should be treated by such remedies as are caluclated to raise the blood pressure.

Exhibition of Appendices showing unusual Conditions. DR. BURNAM.

(To appear later.)

November 16, 1903.

The meeting was called to order by the President, Dr. Futcher.

Aneurism of Arch of Aorta and Innominate. Dr. Osler.

The first case illustrates some points in the symptoms of aneurism of the arch and the innominate artery. The patient was admitted on November 9 from Columbia, S. C. The family history is negative. In his personal history the one important item is that he had lues 8 years ago. He has been a temperate man except in the matter of eating. Two years ago the present trouble began with pain in the right shoulder, neck and arm, the pains being intermittent and lasting from one to two weeks. At the same time, he noted some puffiness of the feet and eyelids and he had a short hacking cough. The pain became more severe and was particularly bad in February, 1903. In June his voice became husky and in August there appeared a swelling above the manubrium and with the appearance of this tumor the pain and shortness of breath disappeared altogether. On September 23, after distal ligation of the right carotid artery, the tumor began to swell and in six hours, according to his statement, reached its present size. There has been no change in the condition since the operation.

The patient is a fairly healthy young man as you look at his face but as he sits up you see this large tumor mass in the neck reaching almost to the chin, obliterating outlines of the neck and projecting as a rounded ovoid mass fully the size of his fist, and on looking on it carefully you see that it pulsates. On palpation you can feel a very strong heaving impulse with the shock of the first and second sounds but there is no thrill. You can see that it is a large aneurismal sac that has come through the manubrium, has eroded the right sterno-clavicular articulation and has elevated the left sterno-clavicular articulation.

The point of interest is the statement that this large tumor appeared immediately after the operation upon the carotid. He thinks he had no swelling here before that time. The probability of course is that the tumor had already eroded the manubrium and the right articulation and while it was small before the operation of course it could not have eroded the bone in six hours and its sudden growth was simply the sudden expansion of the tumor sac shortly after its final rupture through the bone. I do not remember ever to have seen a reference to a very rapid development of the sac following ligation of the carotid.

The symptoms have been much relieved; he has no pain, shortness of breath or dysphagia but that is a very common result of the expansion of the sac in soft tissues. I would like to call the surgical student's attention to the excellent discussion of the symptoms and differential diagnosis between aortic and innominate aneurism in the new edition of Jacobson's Surgery.

Vasomotor Mottling.—Most of you have noticed that a baby's hands are not purely pink but usually pink and white, a mottled state, patches of hyperæmia, with others of a lighter color and some that are quite anæmic. This condition is also found in individuals who have an active cutaneous circulation; and it may be seen in young girls approaching puberty. In the cases before you the mottling of the skin is not pink and white, but blue and white, and this causes a peculiar appearance.

The patient came in a few weeks ago complaining of a peculiar numbness in the hands and feet. The trouble began in November, 1901, following a severe shock. It began in the left foot, then in the right and spread to the neck and arms. She complains now of numbness of the fingers. The greater part of both feet are bluish and in certain places cyanosed, but interspersed are pale anæmic cells. So intense is the coloring that you would think the blue spots were hemorrhagic; but the slightest touch obliterates them. The whole foot can be rendered anæmic by pressure and then the color very gradually returns. The mottling is also very marked over the lower part of the back. The impress of the hand on these livid spots is left in white and it is sometime before the color reappears.

She has improved somewhat under massage and cold packs, has gained in weight, the nervous symptoms have disappeared and she will probably get entirely well. Dr. Weir Mitchell, I believe, has reported a case very similar to this and I have no doubt there are others in the literature. In slight grades it is not uncommon in the hands and feet but so extensive an affection is rare.

A Case of Generalized Neuritis from Lead. Dr. Thomas

The patient, a man of forty-six, gave a marked alcoholic history, but the definite onset of his illness had occurred about two and one-half weeks after entering an enameling establishment. There was marked delirium at onset, increasing weakness, and some pain in the right shoulder. Distinct blue line in the gums, complete paralysis below the shoulder, absence of reflexes, slight dulness of sensation at the periphery, some muscle tenderness, granular degeneration of the red blood corpuscles, and an irregular temperature were the features of the case. General lead palsy is a rare condition, only about twelve cases having been reported in the literature.

Discussion.

Dr. Hurd.—It is interesting to notice that in cases of lead paralysis those muscles seem to be affected which are most used. Painters use their hands and wrists continually and the main effect of the lead poison is upon those muscles. In smelters where lead enters into the ores smelted and where the laborers use their arms mainly in shoveling it is found that the muscles of the arm are most affected, especially the deltoid.

In a case like this it would seem probable that alcohol had as much to do with the attack as lead because it is difficult to understand how such a tremendous effect could be produced by lead in two or three weeks time only.

A Case of Blastomycetic Infection. Dr. Gilchrist.

This is a very typical case of blastomycetic infection of the skin. The disease began several months ago on the right

wrist as a small pimple which gradually increased in size. At one time as the lesion became larger it was mistaken for a ganglion and the attending physician tried to mash it with his thumb. Later it broke down and took the form of a papillomatous growth. This was followed by other lesions appearing on the wrist, the right thigh and the face. All the patches are distinctly papillomatous and the patient has always been able to squeeze out pus from between the papillae. The lesions itch very much and the patient soon found that by squeezing the pus out considerable relief followed. This mode of treatment caused some of the lesions especially those on the thigh and arm, to gradually disappear but those on the face did not succumb so readily and he presents now 9 or 10 lesions scattered over the face. They are superficial in the skin, rather dry, with sloping edges and distinctly papillomatous; and on squeezing, there exudes from between the papillæ a little, rather sticky, white pus from which a pure culture of the organism may be obtained. Here are specimens of the growths as they appear on agar and on glycerine-agar. The blastomycetes were easily found in the pus when soaked in liquor potassæ and they appeared as doubly contoured refractive budding bodies from 7-10 μ in diameter.

This disease, blastomycetic dermatitis, seems to be much more common in the United States than elsewhere. I have now had five cases under my care, but as many as 14 or 15 cases have been reported by Hyde and Montgomery of Chicago and scattered cases from New Orleans, Philadelphia, San Francisco, Canada, etc., have been reported, whereas only one case has been reported from Italy, one from Germany, one from England and one from the northern portion of India. This case forms a typical example of the affection and I shall pass photographs of three other practically new cases around showing the character of the disease. Section taken from a typical lesion of this patient shows benign hypertrophy of the epidermis, the presence of miliary abscesses in the epidermis and corium and pseudo-tubercles in the corium. Blastomycetes were found in the miliary abscesses in fair number. The disease has to be diagnosed from tuberculosis of the skin and from syphilis. Microscopic examination of the pus after soaking it in liquor potassa at once makes the diagnosis clear as the double contoured refractive bodies are usually easily found. The most satisfactory treatment is the free administration of potassium iodide which has a beneficial effect, even when it does not cure the condition. Lately, curetting and the X-rays have been tried with success.

Metabolism in Pregnancy. DR. SLEMONS.

Dr. Slemons reported the results of studies made on four women whose metabolism was followed for about thirty-five days. The diet was carefully regulated and weighed; all the excreta (including urine, lochia, and milk) were carefully measured and daily estimates were made of the amount of urine excreted and the total nitrogen and ammonia output. The series showed a definite diuresis just before and just after delivery. All the cases showed a tendency of the mother to store nitrogen during pregnancy, and the case that bore live twins emphasized this tendency. The series also showed that during pregnancy there is a tendency for actual storing up of ingested fluid to take place. The ammonia excretion shows definitely that a fetus in utero causes changes in the mother's metabolism. It drops to normal after delivery and tends to become normal when the fetus dies in the womb. Relative suppression of renal activity explains the changes in the amount of excreted urine during and following labor. The diminution in nitrogen output is probably due to impairment of the kidney cells. The high ammonia output at the time of delivery cannot yet be explained. During the puerperium all the cases in Dr. Slemons' series showed a definite diuresis except the one that bore dead twins. There was a rise in the nitrogen output, usually beginning about the second day of the puerperium, and probably due to regressive changes in the mother. The ammonia fell gradually to normal. The series showed that metabolism tends to assume a non-pregnant type when the fetus dies in utero.

DISCUSSION.

DR. HURD.—I think we ought to congratulate Dr. Slemons for the extreme industry and care which he has shown in doing this laborious piece of work and also for the clearness with which he has expressed his conclusions. We rarely have a paper presented to this Society showing such definite conclusions with such clear expression.

DR. EMERSON.—There are several points in connection with this paper which might pass unnoticed except by those who had already been at work in metabolism. Although work on this subject has been going on for about 60 years and it has been a favorite subject we have had but a small series of experiments reported showing the proper accuracy demanded by the scientific chemist and the physiologist. The debt of gratitude which Dr. Slemons has expressed to the nursing department is only just, as I can say from my own experience. We have here the co-operation of a nursing department, which is not only willing but able to do its part of the work, which is very trying at times, and it enables us to do the work here as it can be done in but few other institutions.

The four cases which Dr. Slemons has reported are very typical cases, have been studied with the greatest care over a sufficient length of time, by the best methods, and the results are both interesting and important. We congratulate him upon the work he has accomplished and are very glad that he chose the clinical laboratory as the scene of his work.

NOTES ON NEW BOOKS.

The Practice of Obstetrics. Designed for the use of students and practitioners of medicine. By J. CLIFTON EDGAR, Professor of Obstetrics and Clinical Midwifery in the Cornell University Medical College. 1221 illustrations. (*Philadelphia: P. Blakiston's Sons & Co., 1903.*)

After carefully reading this profusely illustrated work of 1111 pages my first impression was one of disappointment, as I had

looked forward with great interest to its appearance, expecting that it would reflect the originality of its talented author. On the contrary, it differs but little from most of its predecessors, except in being abundantly illustrated and laying greater stress upon the necessity for asepsis and emphasizing the serious consequences of its neglect. A decided departure from the usual models is a section on rape and sexual hygiene, as well as a more extended consideration of ante-natal pathology and the diseases of the new-born child than is usually given in obstetrical textbooks.

The book presents a number of serious defects, though it is a perfectly safe guide for both students and practitioners, especially so far as the practical side of obstetrics is concerned. In general it may be said to be open to particular criticism in four respects, namely; verbosity, absence of sound histological and pathological details, a distinct leaning to medical rather than surgical methods of treatment, and an almost entire lack of reference to authorities.

The work could have been condensed with advantage by several hundred pages, partly by the omission of certain subjects, but particularly by greater brevity and lucidity in description. Thus, in not a few places almost equal attention has been devoted to good, bad or indifferent theories or methods of treatment, thereby sometimes leaving the reader in doubt as to which is advocated. That the author was conscious of this defect is shown by the fact that he has thought it necessary to give a résumé or recapitulation of his views at the conclusion of a number of sections.

Another criticism is that not a few subjects are considered in a number of places. Thus, the treatment of occipito-posterior presentations is taken up under the mechanism of normal labor, dystocia from faulty attitude and obstetric surgery. Such repetition tends to make the subject less clear than if it were considered in its entirety in one place.

The work contains 1221 illustrations, many of which are excellent and original with the author and give evidence that great care and considerable thought was devoted to their preparation. Not a few, however, were taken from other sources, for which credit is usually omitted, thereby giving the impression that the author considers that the redrawing of an illustration entitles it to be classed as original. On the other hand, a considerable number are practically useless and could have been omitted with advantage.

A much more serious defect is the faulty description of many histological and pathological conditions. Thus, for example, the yellow color of the peripheral layer of the corpus luteum is attributed to the presence of hematin derived from the central blood clot, instead of to the characteristic pigment lutein, which is formed in the lutein cells before hemorrhage occurs.

The value of the book would apparently have been increased had greater attention been paid to illustrating the section on the placenta and its membranes. For example, there is no satisfactory illustration of the decidua, the only one given being one of Minot's showing the decidual cells of the compact layer. Nor are there any illustrations showing the minute structure of the chorionic villi, the character of whose epithelial covering is left to the imagination of the reader. If the book were scantily illustrated this would, of course, be a minor criticism, but in view of the abundance of illustrations, it would seem that attention could have been devoted to these subjects more advantageously than to some others which are profusely illustrated.

The pathology and history of deciduoma malignum, hydatidiform mole and placental infarcts are treated in an unsatisfactory manner, and the casual reader might readily obtain the impression that the hydatidiform mole is merely a myxoma of the chorion, instead of a complicated growth in which the chorionic epithelium plays a most essential and striking part.

The description of placental syphilis likewise leaves a good deal to be desired. The author does not believe that the changes in the villi are at all constant and that, therefore, their microscopic examination is of little value from a practical point of view. Personally my experience has been quite the contrary. Moreover, he holds that the most constant and characteristic lesion is the presence of gummata; a view which at present has few adherents, as most of the structures which have been described as such are merely infarcts in various stages of degeneration. He also believes that their presence predisposes to retention of the placenta and states that "the greatest maternal risk occurs at the time of labor from adherent placenta and subsequent sepsis." In several hundred syphilitic placentæ, I have never seen any evidence of gumma formation, nor have I noted any particular abnormality in the third stage of labor, but rather the reverse.

Eclampsia is classed among the diseases of the urinary tract, thus giving a false idea as to its nature. The author's views as to its pathology are extremely vague and are as follows: "The pathology of this condition is most obscure. Post-mortem examination of the organs shows general anemia, a congested cerebral cortex, now and then slight apoplexies of the liver and a fluid condition of the blood. It is interesting to note, however, that the most important alterations, decreased urinary toxicity and corresponding increase in the amounts of poisons circulating in the blood are found more strikingly intra vitam than after death." These statements reveal a surprising lack of respect for the work of Schmorl and his followers,who have shown that necrotic lesions of the liver, due to thrombotic processes originating in the periportal vessels, are the most striking manifestations of the disease. Likewise, the statements as to the toxicity of the urine and blood serum are not in accord with the views of most recent investigators, who have discredited Bouchard's work upon the subject and are inclined to attribute the supposed changes to bacterial contamination. While the author has accepted the toxemic origin of eclampsia in its entirety, it would seem that he has failed in great part to apply it to various other complications of pregnancy, such as uncontrollable vomiting and pernicious jaundice.

In the section on extra-uterine pregnancy the anatomical considerations are not in accord with the most modern teachings. Thus, the author considers that rupture is the most frequent termination of tubal pregnancy, and fails to mention the fact that recent investigation has shown that it occurs less frequently than tubal abortion, a condition to which he devotes only a single line. His description of the mechanism of rupture is likewise faulty, as he attributes it to injury of the chorionic villi, rather than to the occurrence of hemorrhage into tissues which have undergone degenerative changes as the result of the corrosive action of the fetal ectoderm. He likewise believes in the possibility of primary abdominal pregnancy, in spite of the fact that not a case has been described within the last ten or fifteen years in which satisfactory evidence has been adduced of such an occurrence.

In the section on the pathology of the puerperium, it is stated that super-involution of the uterus is an abnormal and very rare condition, thereby betraying ignorance of the work of Vineberg, Gottschalk and others, who consider it a routine phenomenon in every nursing woman.

It is unfortunate that so little stress is laid upon the bacterial origin of most cases of puerperal insanity, since cultures taken from the uterine cavity during the early stages of the affection almost uniformly reveal the presence of pathogenic bacteria, particularly streptococci. A little further on, it is stated that after pulmonary embolism, air embolism is the most frequent cause of sudden death during the puerperium. After discussing the matter in considerable detail, the author attributes it to the entrance of air into the uterine vessels and fails to mention that not a few competent observers are extremely sceptical as to the serious

consequences of such an occurrence, since bacteriological examination has shown in a considerable number of cases that the air bubbles which were supposed to have been the cause of death were really the result of infection with *Bacillus aerogenes capsulatus*.

In considering the etiology of uterine rupture, it would seem that the author has devoted too little attention to the condition of the lower uterine segment and the epoch-making work of Bandl. Indeed, the anatomical considerations as to its production, in the section upon the changes produced in the maternal organism as the result of pregnancy, are neither as clear nor as full as might be desired.

The medical rather than surgical tendencies of the author may be made apparent by the following references. Thus, in the treatment of eclampsia he ardently advocates the use of glonoin and veratrum viride, while he speaks disparagingly of the benefits to be obtained from venesection and the infusion of salt solution. In fact, he appears to be guided by fear of criticism in the whole question of blood-letting, for in considering its advisability in the treatment of uncompensated cardiac lesions, he states that "venesection would often be useful were it not for its unfavorable moral effects."

Another and more serious manifestation of this tendency is shown by his advocacy of the induction of abortion in cases of absolute pelvic contraction, which he does not hesitate to recommend as an alternative for Caesarean section. In view of the present excellent results obtained by the latter operation, I consider that such treatment is unjustifiable and but little removed from criminal abortion, and hold that all such patients should be allowed to go to full term and then be delivered by Caesarean section, unless some complication threatening life should occur during pregnancy.

Likewise in considering the question of embryotomy he states that there still exists a very considerable field for the operation, and believes that in ninety-nine cases out of a hundred it would be chosen by the family in preference to Caesarean section. It appears to me, however, that such a decision would not be made if the obstetrician felt himself to be a competent operator and placed the merits of the two operations in their true light, as I know from my own experience that the average patient and her family will follow whatever advice may be given, provided they have confidence in their adviser.

Moreover, the author overestimates the innocuousness of embryotomy, stating that in his experience of six cases it was without mortality whereas Bar and Pinard with a far greater experience show that it is not without considerable danger. He likewise gives a false impression as to the relative merits of the two operations by devoting eighteen pages to the consideration of the various methods of embryotomy and only eight to Caesarean section, which might lead unthinking students to believe that the former was usually the operation of choice. This impression is strengthened in the section on Caesarean section, in which considerable space is given to the consideration of the lowest conjugata vera in which embryotomy is feasible, cases being cited in which it was successfully effected in pelves measuring only one and a half inches (3.8 cm.), while the actual indications are considered very briefly. At the same time he states that Caesarean section is always a dangerous operation, and fails to refer to recent statistics which show the very satisfactory results obtained by experienced operators.

It is gratifying to note that the author is not enthusiastic concerning the merits of symphseotomy; although decided exception must be taken to one of his indications, namely: "When the child cannot be born alive, symphseotomy may be conjoined with a mutilating operation even with a conjugata vera as low as 2.13 inches (5.4 cm.)." This is extremely unfortunate advice, as the only justification for the former operation is the hope of saving the child, and recourse to embryotomy simply means that one has attempted symphseotomy under conditions in which it is not considered called for even by its most enthusiastic advocates.

While my criticisms may appear somewhat harsh, I am glad to say that they apply only to a small portion of the work, as in many other respects the surgical recommendations are the most excellent and are in accord with the best teachings. Thus, he is an enthusiastic advocate of laparotomy in extra-uterine pregnancy and rupture of the uterus, but is very conservative concerning its value in puerperal infection. Moreover, his views as to the methods of inducing labor and bringing about *accouchement forcé* are most satisfactory, in that he justly lays great stress upon the necessity of the internal os being obliterated before the latter becomes a safe procedure. He holds that manual is superior to instrumental dilation, even with Bossi's instrument.

His views as to the employment of version and forceps are in general most excellent, although in the latter operation he does not lay sufficient stress upon the advantages of the cephalic application, and while admitting that it is usually the ideal method, he nevertheless describes the pelvic application first, thereby giving the impression that it is to be employed by preference. His views as to the employment of the forceps as a rotator in posterior positions of the occiput are quite correct, though I cannot subscribe to his advice to deliver with the forceps inverted after rotation. Nor can I understand why he recommends its oblique application in deep transverse positions of the occiput, when its adaptation to the sides of the head is quite as readily effected and is attended with most excellent results.

Another great lack in the book is the almost complete absence of reference to the history of obstetrics and to the men who have made it what it is, and it would seem that a student whose instruction had been obtained solely from this source might be almost entirely ignorant of the work of the great fathers of our art. In making this criticism, I, of course, do not claim that such knowledge is necessary to make one a competent obstetrician, but at the same time it must be admitted that ignorance in this respect is to be regretted, as it tends to make the student feel that all knowledge is of comparatively recent origin; whereas many of the older men did work of which we might be justly proud at the present time. Had this course been adopted in American text-books in the past, it is not likely that we should have seen a number of competent obstetricians describe as original the method of applying the forceps in posterior positions of the occiput, which Scanzoni advocated more than fifty years ago.

In this connection it would appear that the author himself seems to attach but little importance to such details, as he describes the Mauriceau method of extracting the after-coming head as "jaw and shoulder traction, or method of Smellie-Veit or Mauriceau method," thereby giving the impression that Smellie and Veit had invented it, instead of Mauriceau; whereas the latter had described it more than fifty years before Smellie's time, while Veit's connection with it was simply to bring it to the attention of his German confrères.

It might appear from the foregoing that I have nothing but fault to find with the book under review, but such is not the case, as in many portions it is extremely valuable. Thus, the section upon the changes in the maternal organism resulting from pregnancy leaves nothing to be desired, with the single exception of the consideration of the contractive ring. Likewise the section upon the fetus and the mechanism of labor is most excellent, and not a few of the pictures accompanying it are real contributions to the subject. The same may be said of the section on the normal puerperium and the care of the woman and child immediately following labor. The section on puerperal infection is likewise well written and based upon sound teaching and practice. With the exception of the objections already

taken, the section on obstetric surgery is extremely good, and my only criticism is that relatively more space has been devoted to minor than to major operations. J. WHITRIDGE WILLIAMS.

A Text-Book of Obstetrics. Fourth Edition, enlarged and thoroughly revised. By BARTON COOKE HIRST, M. D., Professor of Obstetrics in the University of Pennsylvania. Handsome octavo, 900 pages, with 746 illustrations, 39 of them in color. (*Philadelphia, New York, London: W. B. Saunders & Co., 1903.*)

This, the fourth edition of Dr. Hirst's text-book, contains a number of new illustrations from his recent work on Gynecology and many from the more recent German works; the latter, though excellent, represent the woman in the dorsal position for delivery, and some of the maneuvers depicted are quite impossible with the patient in the left lateral position as advocated by the author. The alterations in the text are comparatively slight, though references have in some instances been added for material present in the earlier editions. The old arrangement whereby abortion, intra-uterine pregnancy, etc., are considered before normal labor, and the management of labor before its mechanism, it still adhered to. The exhaustive index is of great value to the reader. From the standpoint of completeness and reference to original authorities the article on puerperal sepsis stands out prominently, and it is surprising to find, after an excellent résumé of the work on the bacteriology of puerperal fever, that no practical use is made of the evident deductions. Routine examination of the lochia of febrile patients is not encouraged. The author believes that "while such an examination is always interesting, it is not always of great practical value from the diagnostic point of view. It might indeed be distinctly misleading" (p. 716). The pathological anatomy is but briefly considered, and the general treatment recommended is the administration of large doses of quinine "to combat a possible malarial infection" and the routine use of the curette accompanied by one or more flushings of the uterine cavity with 1-2000 bichloride solution. The author has in this edition so far recognized the opposition to this procedure that he advises "care . . . to scrape the walls lightly so as not to penetrate the layer of granulation cells under the endometrium." Laparotomy in puerperal sepsis is advocated with rather broader limitations than has been usually accepted; and in this, as elsewhere, the personal experience of the author is the basis of his judgment. The book contains much practical general advice.

A Text-Book of Obstetrics. By J. CLARENCE WEBSTER, M. D. (Edin.), F. R. C. P. E., F. R. S. C., Professor of Obstetrics and Gynecology in Rush Medical College, in affiliation with the University of Chicago. 383 illustrations, 23 of them in colors. (*Philadelphia, New York, London: W. B. Saunders & Co., 1903.*)

The book is well arranged and neatly printed. Heavy type marks the beginning of each topic and would offer considerable facility in the use of the volume for reference, were not many of the subjects too scantily treated to make the book valuable in this respect. The text abounds in the mention of those who have made contributions to the various sides of obstetrical science, and it is to be regretted that the author has not made his wide reading available for others by appending a bibliography to each chapter.

No consideration of the anatomy of the normal female is supplied. The book opens with the conventional description of the ovum and passes at once to the subject of placentation. This is treated clearly, but too dogmatically, the author's own views frequently taking the place of a fair statement of all sides of a question concerning which authorities differ and where the present state of our knowledge leaves much room for doubt.

The anatomy of pregnancy, labor and the puerperium is better given than in any other text-book written in English. The author's own frozen sections and his study of the reports of others have enabled him to make a presentation of this subject which will repay careful reading.

The abnormal conditions which the obstetrician may be called upon to treat are enumerated at great length and are usually defined with a clearness that is characteristic of the author's style. The pathological and clinical descriptions are meagre. Therapeutic measures are extensively catalogued but without discrimination. The author fails to emphasize the important ones or to condemn the useless ones and rarely states what mode of treatment he has found most satisfactory.

It is surprising to find the author clinging to the pelvic method of application of forceps. Perhaps a little more time and a much better knowledge of obstetrics will be required to apply the blades accurately to the sides of the child's head, but there is ample reward for care in the lessened danger of injury to the mother and to the child.

To hold out anything but the highest ideals to students is surely a mistake. To teach beginners to use forceps with any less information than a painstaking diagnosis can afford, will sometimes lead to loss of life that might be averted. A text-book which not only fails to describe the cephalic method, but merely mentions it for condemnation as ridiculous, is unsafe to place in the hands of men who will rely upon it as their sole source of information.

Tumors, Innocent and Malignant. By J. BLAND-SUTTON, Surgeon to the Chelsea Hospital for Women; Assistant Surgeon to the Middlesex Hospital, London. Third edition. (*Chicago: W. T. Keener & 1903.*)

An extensive review of a work so well and favorably known is unnecessary; however, it might be of interest to mention some of its features.

Excluding those formations known as the infective granulomata, the author arranges tumors in four groups; (1) connective tissue tumors, (2) epithelial tumors, (3) dermoids, (4) cysts.

The subject of sarcoma of bone is well presented. The myelomata are separated from sarcomata and considered in an interesting chapter. This distinction is of importance from the standpoint of their surgical treatment.

The chapters on uterine fibroids have been enlarged and the pathological side of the subject is thoroughly discussed. The chapter on echinococcus colonies has been restored. The chapters on malignant growths of the kidney are well worth reading. In discussing sarcomata of this organ the author mentions their peculiar age distribution, usually their liability to occur in the first five years of life and after thirty years of age.

Probably the most interesting passages in the book are those dealing with the homology of certain tumors and malformations, the occurrence of osteomata in certain fishes, mandibular tubercles in dogs, cervical auricles in goats, bronchial fistulæ in sheep, cutaneous horns in mice, etc.

The important subject of carcinoma of the breast does not receive the careful consideration that it deserves.

The descriptions of the distribution of tumors and the illustrations of their gross appearance are very numerous and very good, but the same cannot be said of the descriptions of their gross and microscopic appearance and the illustrations of the latter. S. H. W.

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